12-2002

Synthetic and structural studies on anticancer agents : C-/O-linked and S-/O-linked hyaluronic acid oligosaccharide mimetics

Qiang Yang
University of Tennessee

To the Graduate Council:

I am submitting herewith a dissertation written by Qiang Yang entitled "Synthetic and structural studies on anticancer agents : C-/O-linked and S-/O-linked hyaluronic acid oligosaccharide mimetics." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

David C. Baker, Major Professor

We have read this dissertation and recommend its acceptance:

David G. Young, Ziling Xue, Hwa-Chain Wang

Accepted for the Council:

Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

To the Graduate Council:

I am submitting herewith a dissertation written by Qiang Yang entitled "Synthetic and Structural Studies on Anticancer Agents: *C*-/*O*-linked and *S*-/*O*-linked Hyaluronic Acid Oligosaccharide Mimetics." I have examined the final paper copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

David C. Baker

David C. Baker, Major Professor

We have read this dissertation
and recommend its acceptance:

Accepted for the Council:

Vice Provost and Dean of
Graduate Studies

SYNTHETIC AND STRUCTURAL STUDIES ON ANTICANCER AGENTS: *C*-/*O*-LINKED AND *S*-/*O*-LINKED HYALURONIC ACID OLIGOSACCHARIDE MIMETICS

A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Qiang Yang

December 2002

DEDICATION

This dissertation is dedicated to my father,
Mr. Wen-Bin Yang,
my mother, Mrs. En-Xia ZuanSun,
and my wife, Hua-Lei.

ACKNOWLEGEMENTS

First and foremost, I would like to express my deepest thanks and sincere appreciation to my research advisor, Dr. David C. Baker, for his guidance, understanding, encouragement and support. I wish to express my deep gratitude to him for his brilliant ideas and invaluable advice, which certainly is not limited in research only. I always consider that conducting research under Dr. Baker's guidance is my great honor.

I am also grateful to Dr. David. G. Young, Dr. Ziling Xue and Dr. Hwa-Chain Wang for serving on my committee. I appreciate their efforts in participating in my original research proposal (ORP) and in generating this dissertation.

Special thanks also go to Dr. Zhong-Xu Ren for his collaboration on the synthesis of *C*-/*O*-linked hyaluronic acid oligosaccharide mimetics project, to Dr. Karen T. Welch for acquiring the 2D NMR spectra, to Benji S. Prebyl for acquiring the mass spectra, and to Dr. Tian-Niu Chen for acquiring the X-ray data.

I would like to thank the many past and present members of the Baker group, particularly Dr. Zhan-Jiang Li, Sarah A. Headrick, Dr. David C. White, Dr. Sean Hamilton, Conrad Kaczmarek, Ambroise Akue, and Riyam Kafri for their assistance and friendship. I am also grateful to the Department of Chemistry at University of Tennessee, Knoxville and National Institutes of Health (NIH) for their financial support.

Last but not the least, I wish to thank my family for their love, encouragement and support.

ABSTRACT

Hyaluronic acid (HA) is a polysaccharide synthesized in the plasma membrane of cells and is associated with the host cell's extracellular matrix. Recent studies have established that HA plays an important role in cancer metastasis by interacting with cancer cell's CD44 receptor and serving as a chemoattractant for establishing metastatic foci. In first generation studies, HA oligosaccharides were found to show profound antimetastatic activity in a B16F10 mouse melanoma model. Our goal was to develop mimetic compounds for the natural HA oligosaccharides that would be resistant to enzymatic degradation and serve as candidates for antimetastatic drugs in the treatment of cancer. Described in this dissertation is the synthesis of *C*-/*O*-linked and *S*-/*O*-linked HA tetrasaccharide mimetics and *S*-/*O*-linked HA hexasaccharide mimetics. The *C*-/*O*-linked HA tetrasaccharide was synthesized in collaboration with Dr. Zhong-Xu Ren via trichloroacetimidate glycosylation of two specifically protected *C*-disaccharides as building blocks, which were obtained by C-coupling reactions of a glycosyl tin derivative and a glycosyl pyridinylsulfone with an aldehyde, promoted by MeLi/BuLi and SmI_2, respectively. The *S*-/*O*-linked HA tetrasaccharide was synthesized via trichloroacetimidate glycosylation of two strategically protected *S*-disaccharides, which were accomplished through base-mediated coupling of a thiol with two different triflates. Based on the chemistry developed in the synthesis of *S*-/*O*-linked HA tetrasaccharide mimetics, the synthesis of *S*-/*O*-linked hexasaccharide mimetics was accomplished via trichloroacetimidate glycosylation from a universal *S*-linked disaccharide unit that is

strategically protected to be used as either a *C*-1 glycosyl donor or as a 3′-OH glycosyl acceptor.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF SCHEMES

LIST OF TABLES

ABBREVIATIONS AND ACRONYMS

Ac	Acetyl
AcOH	Acetic Acid
ADMA	Anisaldehyde dimethyl acetal
AIBN	Azoisobutyronitrile
All	Allyl
Bn	Benzyl
Bz	Benzoyl
Bu	Butyl
n-Bu_3SnH	Tri-*n*-butyltin hydride
CAN	Ammonium cerium(IV) nitrate
COSY	Correlated spectroscopy
m-CPBA	*m*-Chloroperoxybenzoic acid
DIBAL-H	Diisobutylaluminum hydride
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMAP	4-Dimethyaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	Dimethyl sulfoxide
DTT	Dithiothreitol
EDCI	1-(3-Dimethylaminopropyl)-3-ethylcarbdiimide hydrochloride
ESI	Electrospray-ionization
Et	Ethyl
EtOAc	Ethyl acetate
EtOH	Ethanol
GlcA	D-Glucuronic acid
GlcNAc	*N*-Acetyl-D-glucosamine
HA	Hyaluronic acid

HMBC	Heteronuclear multiple-bond correlation
HSQC	Heteronuclear single-quantum coherence
Lev	Levulinoyl
MALDI	Matrix-assisted laser-desorption ionization
MeOH	Methanol
Me	Methyl
MP	*p*-Methoxyphenyl
MS	Mass spectrometry; molecular sieves
NMR	Nuclear magnetic resonance
ORTEP	Oak ridge thermal ellipsoid progrem
PCC	Pyridinium chlorochromate
PDC	Pyridinium dichromate
Phth	Phthalimido
PMB	*p*-Methoxybenzyl
TBAF	Tetrabutylammonium fluoride
TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
TEA	Triethylamine
TEMPO	2,2,6,6-Tetramethyl-1-piperidinyloxy
Tf	Trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
TMS	Tetramethylsilane
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
TOCSY	Totally correlated spectroscopy
TsOH	*p*-Toluenesulfonic acid

I. INTRODUCTION

1.1. Biological Background

Hyaluronic acid (HA), a polysaccharide composed of a repeating disaccharide unit in which D-glucuronic acid is linked to the 3-position of *N*-acetyl-D-glucosamine, i.e., [β-D-GlcNAc-(1→4)-β-D-GlcA-(1→3)]$_n$, is synthesized in the plasma membrane and is associated with extracellular metrix (as shown in Figure 1).[1] Recent studies have established HA as an increasingly important bioactive polysaccharide that has potential important in medicine. As a result of its unique pyhsicochemical properties, HA has found use in drug delivery, as an antiadhesive, in opthamatic tissue replacement, and in osteoarthritis therapy application.[2-4] However, the most significant roles are those it has been shown to play in cancer.[5-7]

As we know, cancer as a disease is characterized by (1) uncontrolled cell growth, (2) a lack of cell differentiation, (3) invasion of other neighboring tissues, and (4)

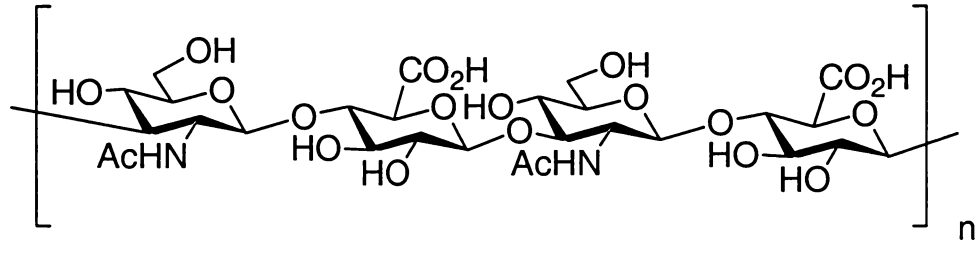


Figure 1. Hyaluronic Acid (HA).

metastasis–the ability to establish new foci at site remote from the primary neoplastic growth.[8] Metastasis itself is a complex series of events that require the cell to (1) loosen its adhesion from its primary cell (tumor) neighbors, (2) migrate through tissues to reach a blood vessel, (3) cross the basal lamina and endothelium of the blood vessel to enter the general circulation, (4) adhere to the cell wall in a new tissue, (5) extravasate by crossing the basal lamina, and (6) migrate through the surrounding tissue to gain a colonization foothold.[9-12] These processes appear to be mediated by interactions between cell-adhesion molecules on the cancer cell and structural elements on the host cell.[13] The major participants in this cell–cell adhesion process have been identified.[14] Processes involving protein–protein interacting,[15] as well as sialic acid-E-selectin binding,[16] have been demonstrated. Recent studies discovered that HA plays an important role in stages (2) and/or (6) by interacting with the tumor cell's CD44 receptor (CD = "cluster of differentiation").

The interaction between HA and CD44 receptor is complex and is still not fully understood. Early evidence indicates that HA facilitates tumor-cell migration. HA is extruded into the extracellular space where it is hydrated and expands the intercellular space which facilitates cell movement along HA-enriched tracks in the expanded space.[17,18] Carcinomas are usually associated with the production of large quantities of HA that is located primarily at the interface of the tumor and the surrounding normal tissue,[19-21] and malignant tumors express high levels of HA-binding receptors.[22,23] Several lines of evidence further implicate a CD44–HA interaction in cancer metastasis.[24-29] CD44 is a transmembrane glycoprotein that plays important roles in angiogenesis,

cellular adhesion and migration, hyaluronate degradation, lymphocyte activation, and macrophage aggregation.[30] Due to the mechanism of variable splicing during transportation, CD44 is actually expressed as a number of isoforms that can vary from one tissue to another. All CD44 isoforms appear to have the potential for binding to HA.[31]

Based on these studies, a metastasis model is depicted in Figure 2: Migrating cancer cells release paracrine growth factors that induce host cells in adjacent stroma to produce increased amounts of extracellular HA. The cancer cells then make use of their CD44 receptors to bind to and migrate along the newly synthesized HA tracks into new tissues, spawning metastases. The interest in cancer-related CD44–HA interaction is broad and not limited to the particular scenario of the melanoma-lung focused upon by our biological model. A number of reports have provided further evidence that HA–CD44 binding is involved in several different types of neoplastic growths such as pancreatic,[32] ovarian,[33,34] breast,[35] colon,[36] prostate,[37] and brain[38,39] cancers.

1.2. Biological Evaluation of HA Oligosaccharides as Metastasis Inhibitors

Based on these studies, we proposed to use HA oligosaccharides as CD44 "metastasis receptor" antagonists since, if HA polysaccharide strands are used as "tracks" for cancer cell migration, then small HA oligosaccharides should inhibit the binding of CD44 to the tracks, thus block metastasis (as shown in Figure 3). This therapeutic approach, if successful, would be refreshingly novel, as it would involve essentially cell-surface phenomena and would not make use of cytotoxic agents that involve the cell

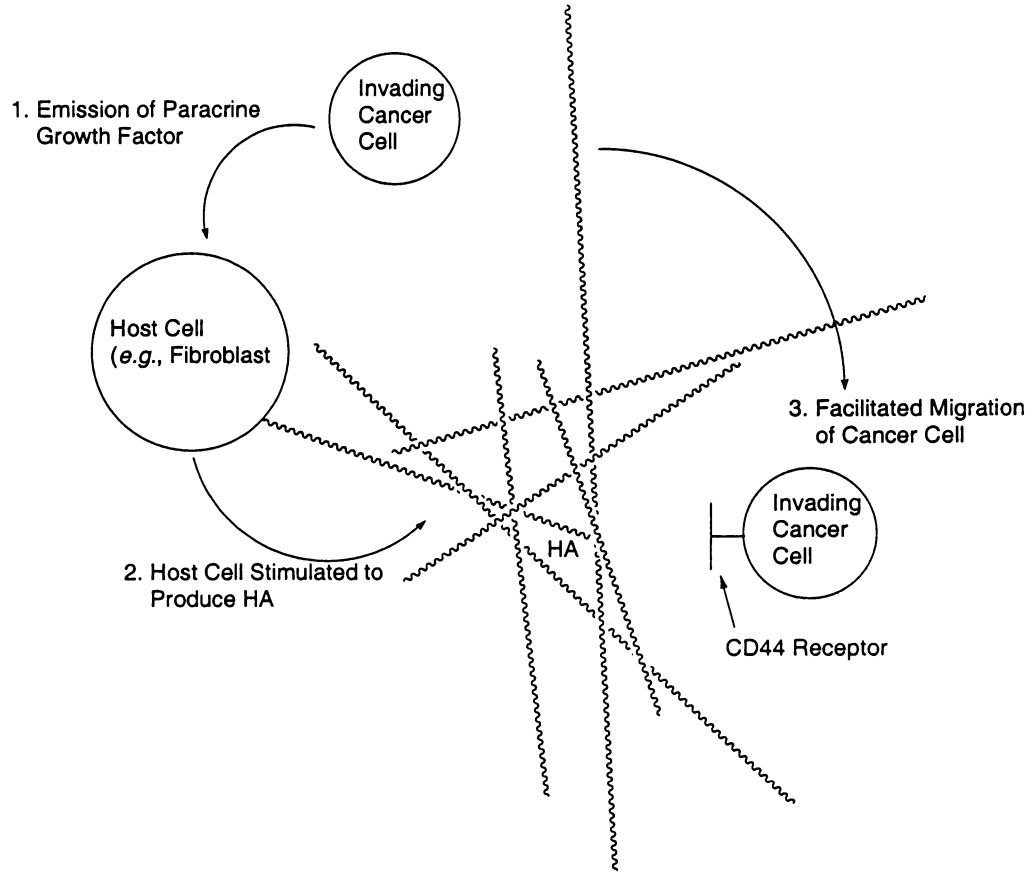


Figure 2. Current Model of HA/CD44-Mediated Cancer Cell Metastasis.

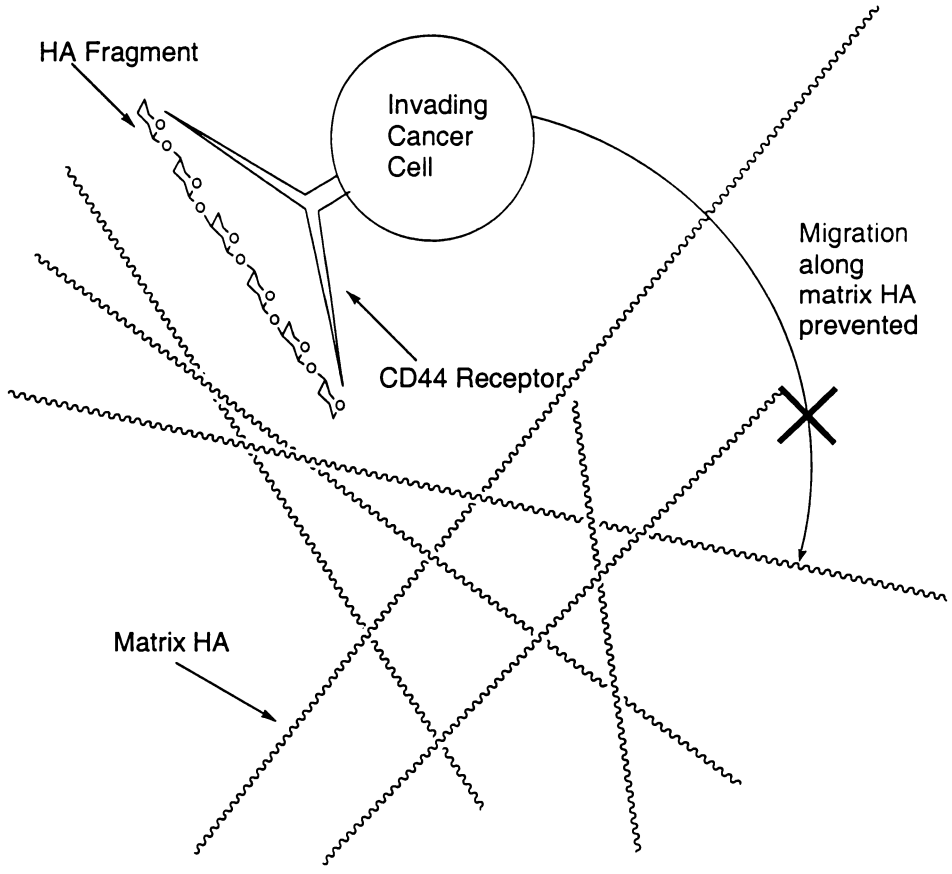


Figure 3. Pharmacological Intervention in Metastasis.

cycle. One could envision a therapeutic approach that would involve either surgical removal or radiation therapy on the primary tumor, followed by treatment with a CD44 antagonist that would, in cases of highly metastatic tumors, prevent metastasis. In cases of highly metastatic forms of cancer, a metastasis inhibitor could prolong life, especially in cases where the primary tumor is untreatable. Such an approach using non-HA type compounds as ligand-mimicking drugs to effectively block cancer-cell adhesion has been suggested for patients at high risk of metastasis.[40-42]

To support our hypothesis, a set of experiments were carried out by our collaborator, Dr. Richard Cysyk and co-workers, as follows:[43] (1) HA was degraded with hyaluronate lyase (EC 4.2.2.1) from *Streptomyces hyalurolyticus*. (2) The resulting oligosaccharides were incubated with B16F10 melanoma cells *in vitro* (10^5 cell count), and the mixture was then injected i.v. (tail vein) into mice. In the control set of experiments, the mice were injected with only B16F10 melanoma cells. (3) After ten days, the lungs of the mice of both groups were excised and examined for metastatic colonies. It was anticipated that a reduction in metastasis would be observed in the mice that received pretreated melanoma cells with HA oligosaccharides. To our amazement there was not only a reduction, but a near-total absence of metastatic colonies in the lungs of the mice receiving pretreated B16F10 melanoma cells with HA oligosaccharides. The experiment has been repeated with identical results using a verity of controls to ascertain that the result is genuine. B16F10 cell viability in the HA-oligosaccharide-treated sample was checked, as well as various controls of column effluent, buffers, etc.. To identify possible toxic effects of the digest on the melanoma cells, experiments using double and

triple the amount of HA oligosaccharides (up to 3 mg/mL) were carried out, and no toxicity was found (as determined by cell viability assays). A similar experiment with HA itself (1 mg/mL) shows an antimetastastic effect; however, the fact that the purified oligosaccharides (free of HA) are active as metastasis inhibitors indicates that a relatively small molecule can function as an antimetastatic probe, which is essential to our research. Preliminary studies show activity setting in with the 8-mer.

1.3. Design of Hydrolase-Resistant Mimetics of HA Oligosaccharides

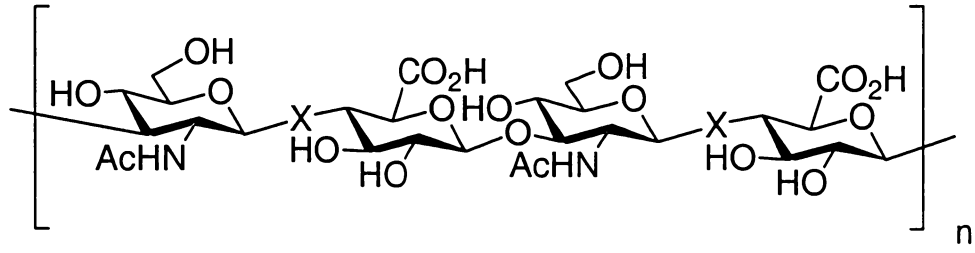
It is well known that HA is degraded in the local tissues where it is produced, as well as in the lymph and in the liver.[44,45] Degradation may be initiated by the receptor-mediated process whereby the CD44 receptor binds to HA, after which it is endocytosed, transferred to a lysozome, and degraded by acid hydrolases.[46,47] In addition, degradation pathways via extracellular hyaluronidases are also suspected.[48] In mammals, the degradation is accomplished by three enzymes: Hyaluronidase (EC 3.2.1.35), β-D-glucuronidase (EC 3.2.1.31), and 2-acetamido-2-deoxy-D-hexosaminidase (EC 3.2.1.30).[49] Hyaluronidase is an *endo*-glycosidase specific for the glycosidic bond β-D-GlcNAc-(1→4)- β-D-GlcA; while the β-D-glucuronidase and 2-acetamido-2-deoxy-D-hexosaminidase are *exo*-glycosidases that remove a GlcNAc or a GlcA residue from the nonreducing end of the polymer respectively.

An oligosaccharide that would foil the degrading enzymes would ideally be one in which the glycosidic –*O*– linkages are replaced with –CH_2–. Such *C*-glycosylic compounds are known to conformationally mimic their *O*-glycoside counterparts and are

resistant to enzymatic cleavage.[50] However, such compounds are difficult of synthesis, the degree of difficulty increasing with the number of sugar units in the target compound. To date, the largest *C*-oligosaccharide is but a *C*-trisaccharide; hence, a *C*-oligosaccharide of four or more units for use as readily available probe or drug candidate is, at present, out of question. Therefore, rather than synthesizing an entirely *C*-linked oligosaccharide, we would design a "mixed" oligosaccharide, in which the vulnerable (1→4)-*O*-linkages will be replaced with *C*-linkage so that the oligosaccharides would be safe from enzymatic hydrolysis, while the (1→3)-linkage would be a regular *O*-linkage, mainly to facilitate ready synthesis, as the chemistry of glycosides is the most well-documented displine in carbohydrate chemistry.[51]

In addition to the $-CH_2-$linked oligosaccharides, –*S*–linked compounds, known as thioglycosides, could also be considered. Thioglycosides are well studied compounds because of their utility as C-1 activator groups in glycosylation reactions.[52,53] Thiooligosaccharides are considerably easier of synthesis than their *C*-linked counterparts.[52] These are generally known to confer hydrolytic stability to the glycosidic linkage;[54] however, to our knowledge no one has evaluated these types against hyaluronidases and related oligosaccharides. Candidate compounds are shown in Figure 4.

The principal asset of this approach—"mixed" oligosaccharides—is their ready accessibility through a convergent "block synthesis" approach wherein multiple copies of a single *C*-linked (or *S*-linked) disaccharide are linked *n* times via normal glycosidation techniques to produce oligomers of specified length (of either 4, 6, or 8 residues, etc.). The choice of a GlcNAc–X–GlcA block unit over the other possible units (e.g., the



X = S, CH_2.

Figure 4. Mimetics of HA Oligosaccharides.

GlcA–X–GlcNAc unit) was made, as this repeat unit removes any vulnerability to glucuronidase activity.

II. STATEMENT OF THE PROBLEM

2.1. Objectives

Our synthetic goals are as follows:

1. Synthesis of *C*-/*O*-linked HA Tetrasaccharide Mimetics
2. Synthesis of *S*-/*O*-linked HA Tetrasaccharide Mimetics
3. Synthesis of Higher Order *S*-/*O*-linked HA Oligosaccharide Mimetics

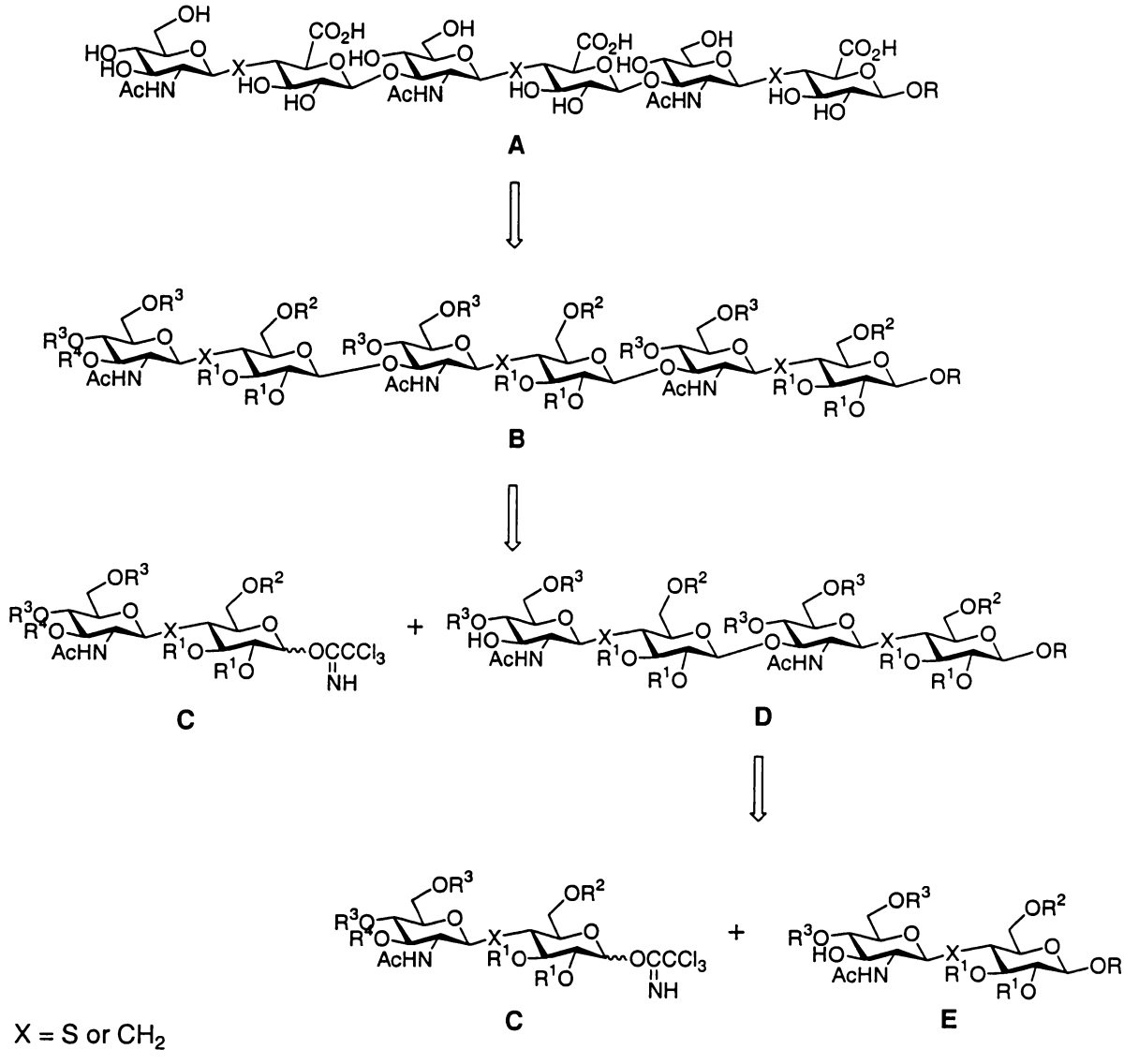
With respect to the synthesis of *C*-/*O*-linked HA oligosaccharide mimetics, we would focus on the synthesis of a properly protected *C*-linked disaccharide that would serve as a building block of the synthesis of higher order *C*-/*O*-linked HA oligosaccharide mimetics. The disaccharide, once synthesized, will be handed over to my co-worker, Dr. Zhong-Xu Ren, for completion of the synthesis of *C*-/*O*-linked HA tetraaccharide mimetics. Since the chemistry of the synthesis of *S*-linked oligosaccharides is well documented compared to that of *C*-linked compounds, our efforts would mainly focus on the synthesis of *S*-/*O*-linked HA tetrasaccharide mimetics which would (1) allow us to investigate the chemistry for the synthesis of higher order *S*-/*O*-linked HA oligosaccharide mimetics, (2) provide us the material for NMR and molecule modeling studies, and (3) allow us to study the resistance to degradation by HA-degrading enzymes. With a small protecting group modification of the *S*-disaccharides for the *S*-/*O*-linked HA tetrasaccharide mimetics, we would adapt this chemistry to the synthesis of *S*-/*O*-linked HA hexasaccharide mimetics and beyond.

2.2. Research Plan—Retrosynthetic Analysis

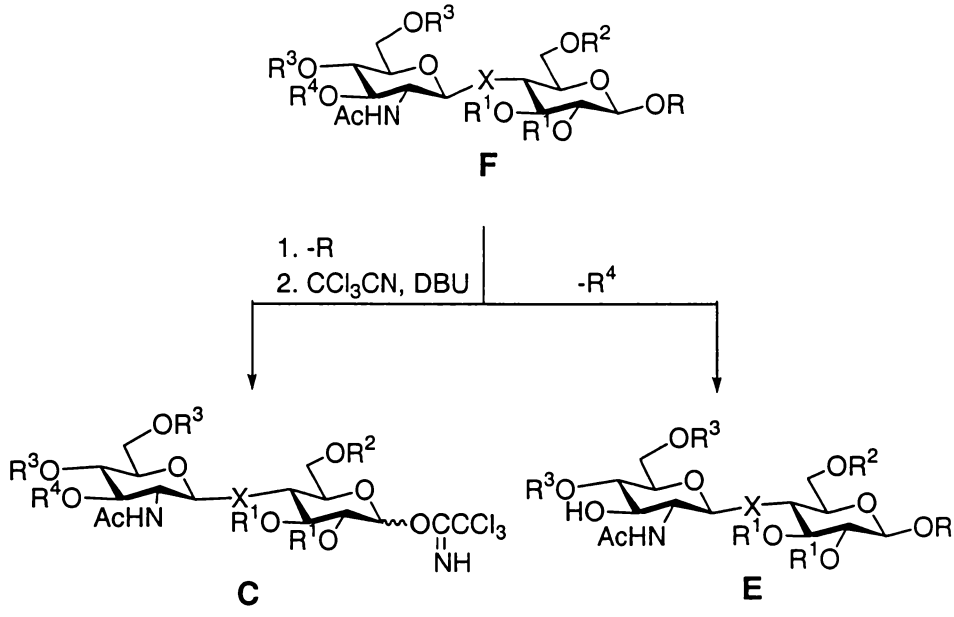
A retrosynthetic analysis for the synthesis of *S-/O-* and *C-/O-* "mixed" linked oligosaccharides is shown in Scheme 1. The oligosaccharides will be built up via Schmidt's trichloroacetimidate glycosylation from a versatile GlcNAc-X-GlcA unit that is strategically protected to be used as either a glycosyl acceptor (3'-OH free) or as a C-1 glycosyl donor (1-OH free), activated as a trichloroacetimidate (as shown in Scheme 2). *X*-linked disaccharide trichloroacetimidate **C** reacts with disaccharide acceptor **E** to afford the tetrasaccharide, which after selective removal of R^4 would serve as an acceptor **D**. This tetrasaccharide acceptor is resubjected to trichloroacetimidate **C** to afford hexasaccharide **B**. In theory, higher order oligosaccharides could be obtained by repeating the selective removal of R^4 and glycosylation. Furthermore, the GlcA moiety is protected to allow selective 6-deprotection-oxidation to glucuronic acid (6–CO_2H group) at a late stage in the synthesis. This basic strategy will allow the glycosidic linker to be either *–S–* or *–CH_2–*. Some fine tuning of this general strategy—mainly the selection of optimum protecting groups for *–S–* vs. *–CH_2–* series of compounds—has been necessary once we began actual synthetic work.

2.3. Synthesis of *C-/O*-linked HA Tetrasaccharide Mimetics

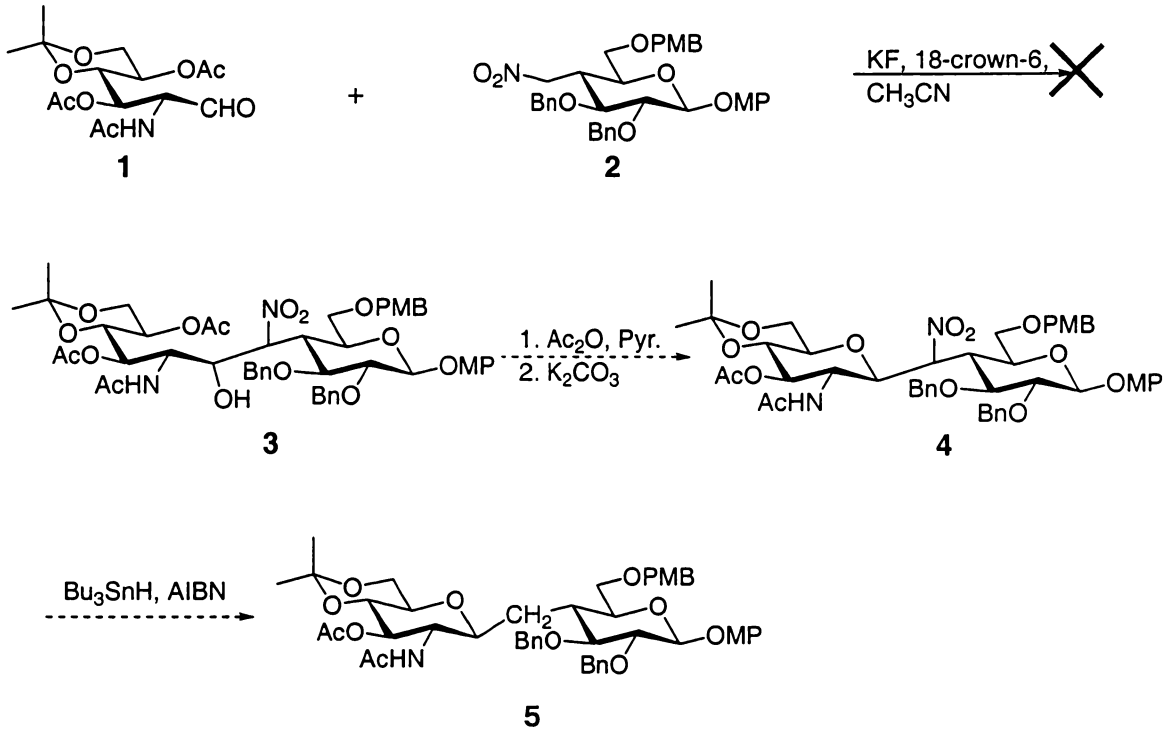
In our group's previous work,[55] Martin's method[56,57] (as shown in Scheme 3), as well as an intramolecular radical coupling via the condensation of phenylseleno amino sugar and 4-*C*-methylene-*β*-D-xylo-hexopyranosiduronic acid[58,59] (as shown in Scheme



Scheme 1. Retrosynthetic Analysis.

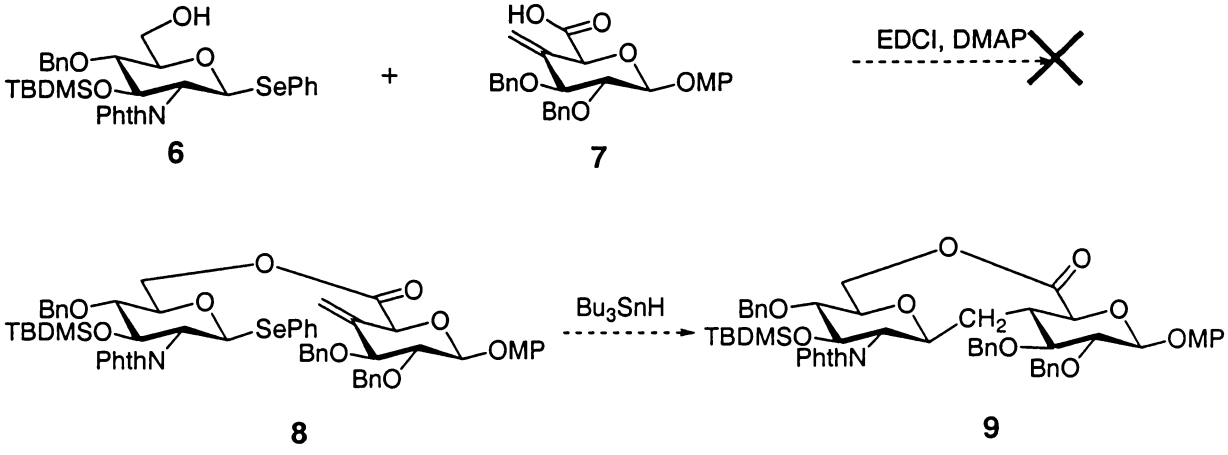


Scheme 2. Disaccharide Building Blocks.

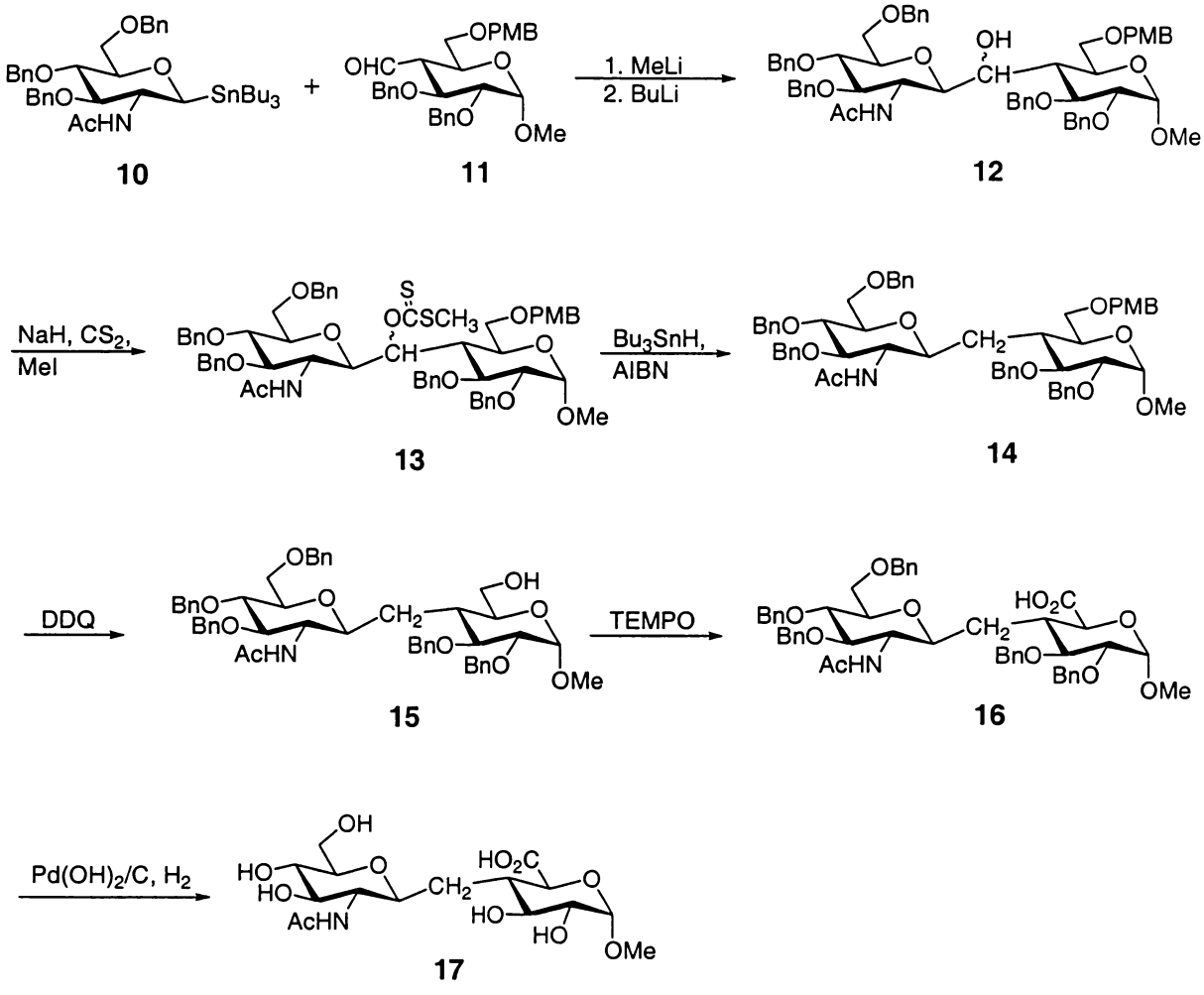


Scheme 3. Our Group's Previous Approach to *C*-linked Disaccharides.

4), was investigated, which gave no desired results. A *C*-linked HA disaccharide mimetic, albeit via Kessler's dianion method (as shown in Scheme 5),[60-62] was successfully obtained.[63] However, problems presented in the modification of protective groups (to free 3'-OH) as several severe conditions were involved in the preparation of starting materials as well as in the coupling reaction. In Beau's recent studies,[64,65] the synthesis of α-*C*-glycosides via the coupling of 2-acetamido-3,4,6-tri-*O*-benzyl-1,2-dideoxy-1-pyridinylsulfonyl-α-D-galactopyranose with aldehydes or ketones under the promotion of samarium diiodide was desicribed. We suspected that the β-2-pyridinyl sulfone would give predominantly β-*C*-glycosides. Furthermore, this method also raises the possibility of modifying the protective groups since the reaction conditions are relatively mild. However, their efforts to synthesize a 2-acetamido-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose resulted in a very low yield, while coupling reactions involving C-2-azido or C-2-benzylcarbamoyl functionality afforded no desired *C*-glycosides. To this end, no reactions involving 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose (**20**) have been reported. Therefore, at this stage, our main efforts are devoted to (1) developing a route to the appropriately protected 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose (**20**), (2) investigating the chemistry for the synthesis of β-*C*-linked disaccharides via the reaction of appropriately protected 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose (**20**) with appropriately protected aldehyde **21** under the promotion of samarium diiodide (SmI_2), and (3) using the disaccharide thus



Scheme 4. Our Group's Previous Approach to *C*-linked Disaccharides (cont'd).



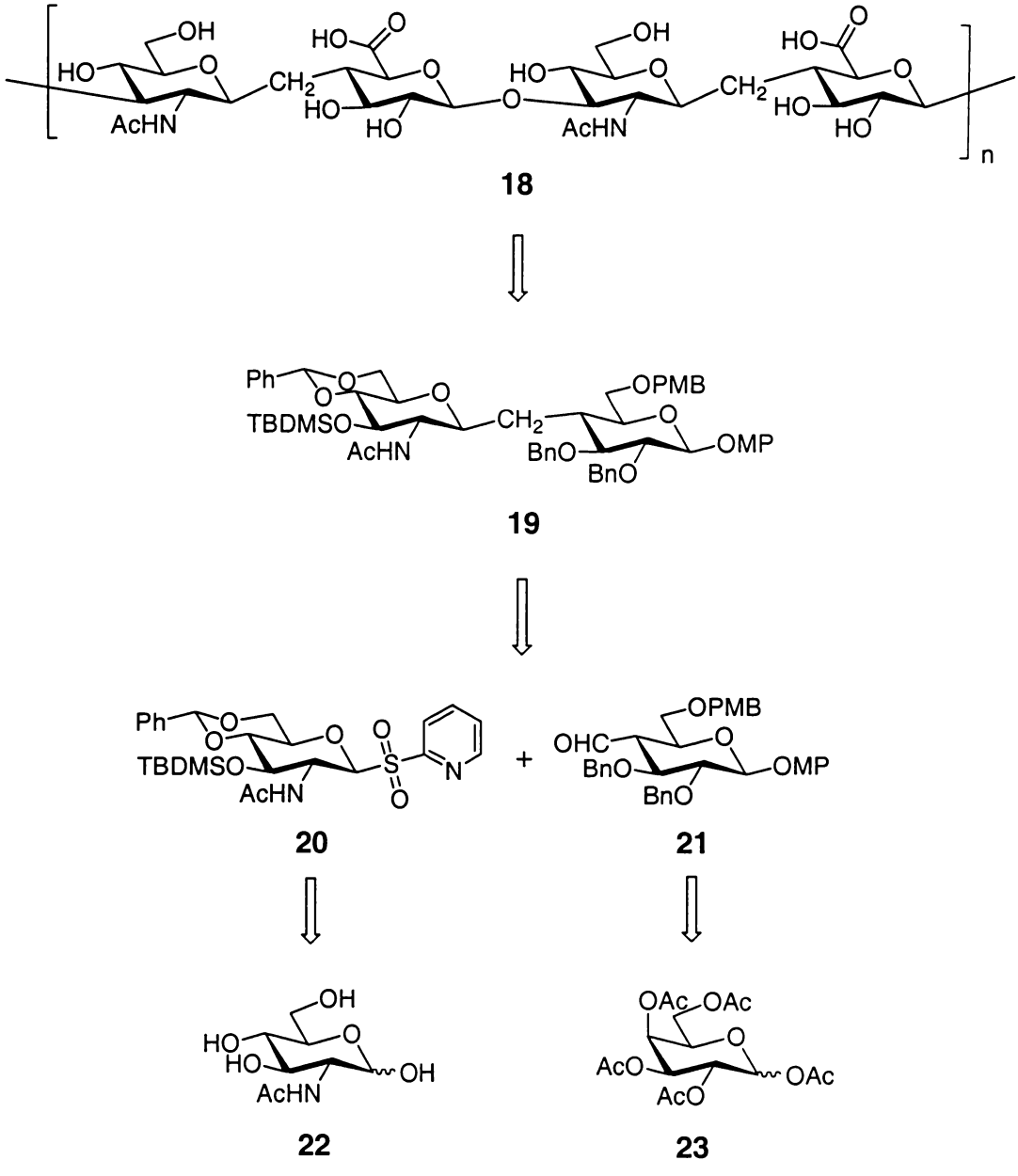
Scheme 5. Our Group's Previous Approach to *C*-linked Disaccharides (cont'd).

obtained as a building block to synthesize *C*-/*O*-linked HA tetrasaccharide mimetics.

A retrosynthetic analysis is shown in Scheme 6. Glycosyl donor, the sulfone **20**, will be prepared from commercially available compound, 2-acetamido-2-deoxy-α-D-glucose (**22**). According to our group's previous work,[66] glycosyl acceptor, aldehyde **21**, could be synthesized from commercially available D-galactose pentaacetate (**23**). Sulfone **20** will be reacted with aldehyde **21** under the promotion of samarium diiodide (SmI_2) to afford disaccharide **19**. The protective groups' pattern in disaccharide **19** satisfies the requirements for the synthesis of higher order *C*-/*O*-linked HA oligosaccharide mimetics. Hence, *p*-methoxyphenyl (MP) group could be selectively unmasked with ammonium cerium(IV) nitrate (CAN) in the presence of all the other groups.[67,68] A glycosyl donor could be obtained if the resulting disaccharide is activated as the trichloroacetimidate; while the *O*-*tert*-butyldimethylsilyl (*O*-TBDMS) could be deprotected with tetrabutylammonium fluoride (TBAF) to afford a glycosyl acceptor.[69] Furthermore, the GlcA moiety is protected to allow selective 6-deprotection–oxidation to the glucuronic acid (6–CO_2H group) at a late stage in the synthesis.

2.4. Synthesis of *S*-/*O*-linked HA Oligosaccharide Mimetics

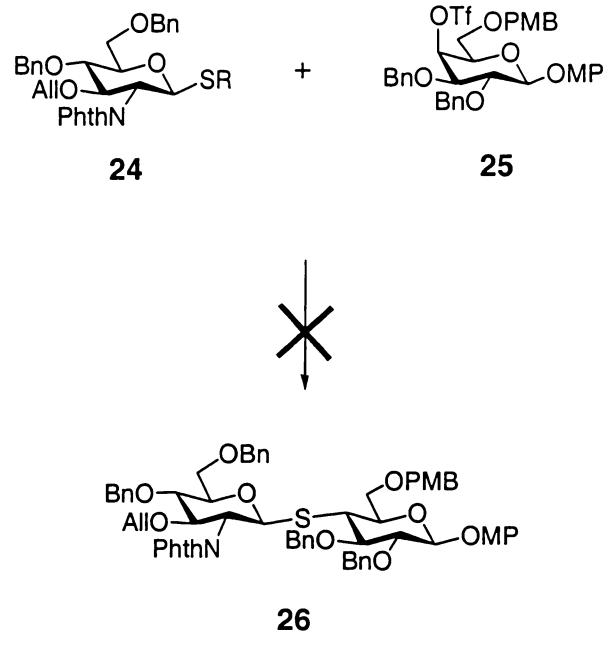
The requisite chemistry to the *S*-/*O*-linked HA oligosaccharide mimetics requires that four levels of differential protection be implemented: (1) selective manipulation of C-6 oxidation, (2) sulfur-atom introduction, (3) selective deprotection of the glycosyl acceptor, and (4) activation of the glycosyl donor site. In our group's previous work,[66] a route based on chemistry developed by Driguez and co-workers[70-72] in which a 1-



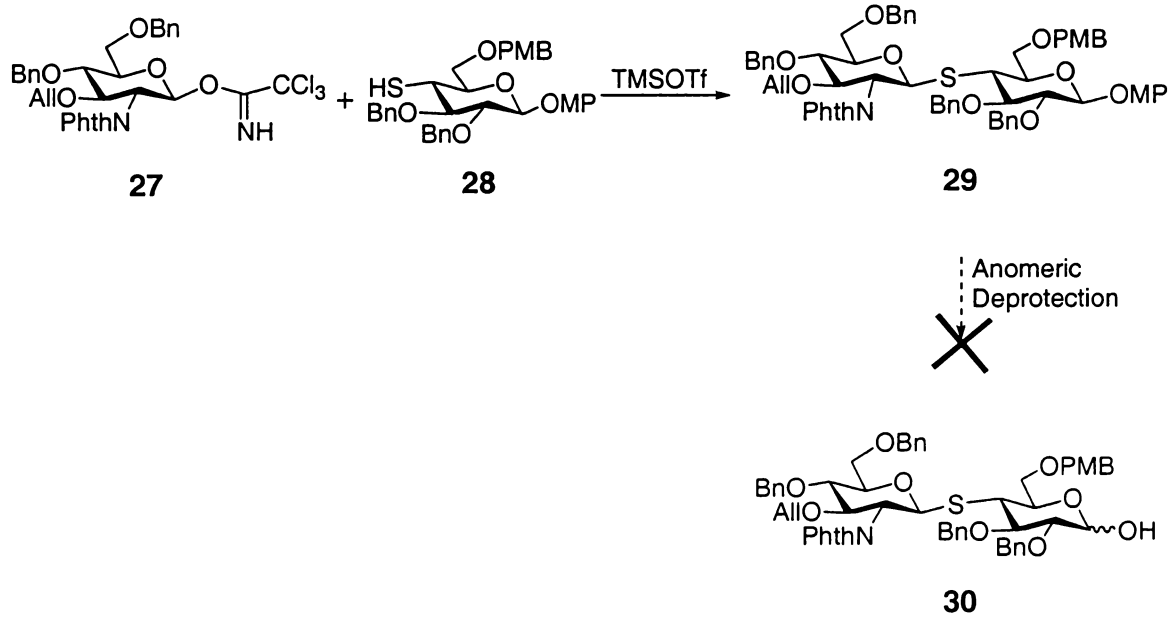
Scheme 6. Retrosynthetic Analysis of *C*-/*O*-linked HA Oligosaccharides.

thiosugar (Gly-SH) displaces an axial 4-*O*-triflyl group of a protected galactose moiety was investigated. Unfortunately, the reaction that involved a complicated *N*-phthalimido derivative did not work, owing no doubt to complex stereochemical interactions between the reactants (as shown in Scheme 7). An alternative route, however, has been developed, albeit via the less common "reverse strategy" of reacting a 4-SH glycosyl acceptor with a suitably activated glycosyl donor, a trichloroacetimidate. However, protective-group manipulations of intermediate **29** suffered from low yields and other problems (as shown in Scheme 8). With a small protective group modification, an alternative *S*-disaccharide was obtained. In this case, although the anomeric deprotection was successfully achieved, problems arose in deacetylation to give the free 3'-OH and activation of the disaccharide as the trichloroactimidate (as shown in Scheme 9).

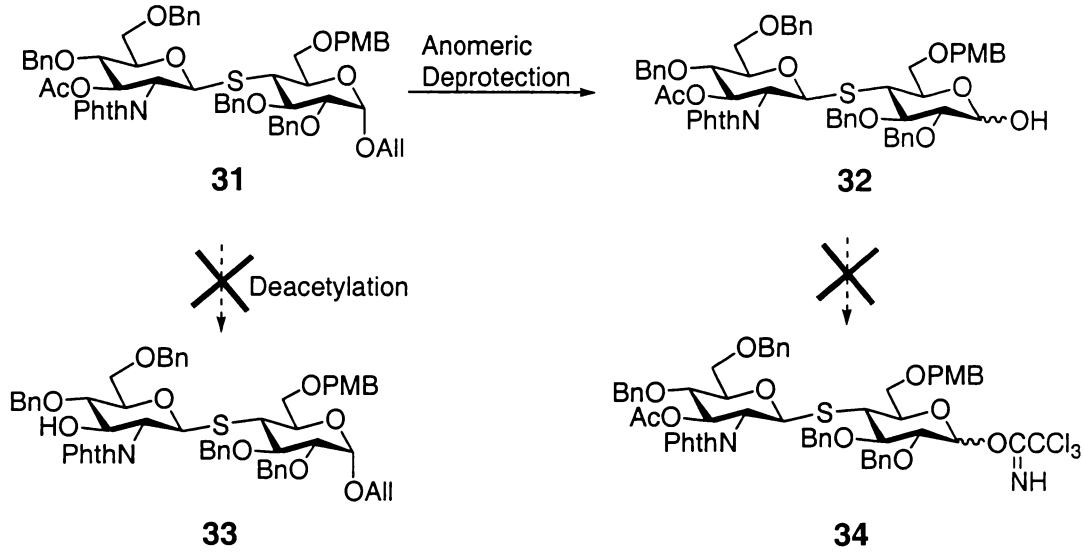
Recent years saw several papers devoted to this topic. Yuan C. Lee and co-workers[73] reported the synthesis of *S*-linked tetrasaccharides via the condensation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-*β*-D-glucopyranose with triflates under the promotion of sodium hydride or cysteamine (as shown in Scheme 10). Similar reactions were also reported by France-Isabelle Auzanneau and co-workers (as shown in Scheme 11). [74] This chemistry could be employed in our project with modification of the protective groups. In our group's previous work,[63] an *S*-linked HA disaccharide mimetic has been successfully synthesized via the condensation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-*β*-D-glucopyranose with methyl 2,3-di-*O*-acetyl-6-*O*-*tert*-butyldimetylsilyl-4-*O*-trifluoromethanesulfonyl-*β*-D-galactopyranoside in the presence of cesium carbonate(Cs_2CO_3). However, as restrained by the protective groups, the



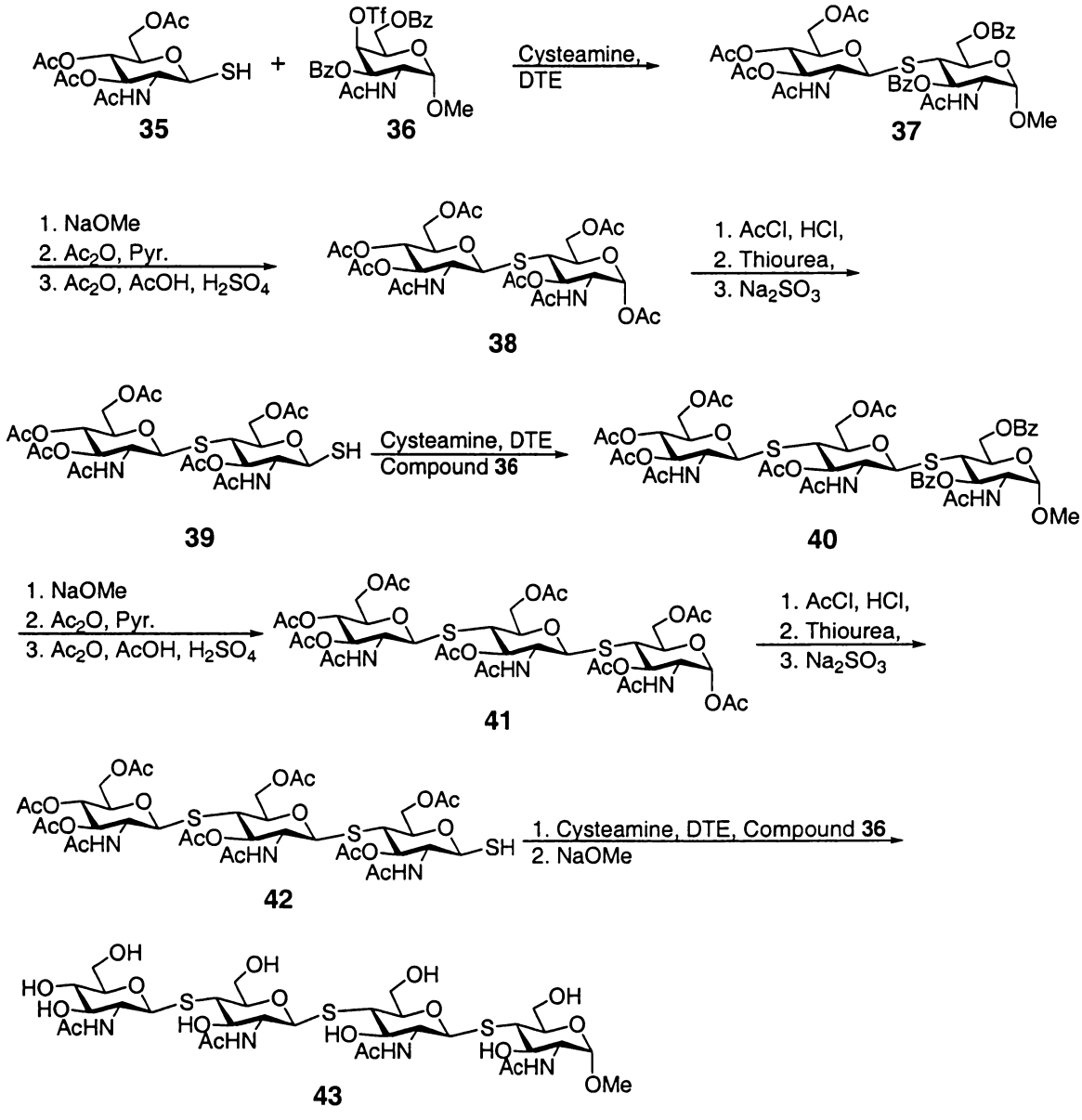
Scheme 7. Our Group's Previous Approach to *S*-linked Disaccharides.



Scheme 8. Our Group's Previous Approach to *S*-linked Disaccharides (cont'd).

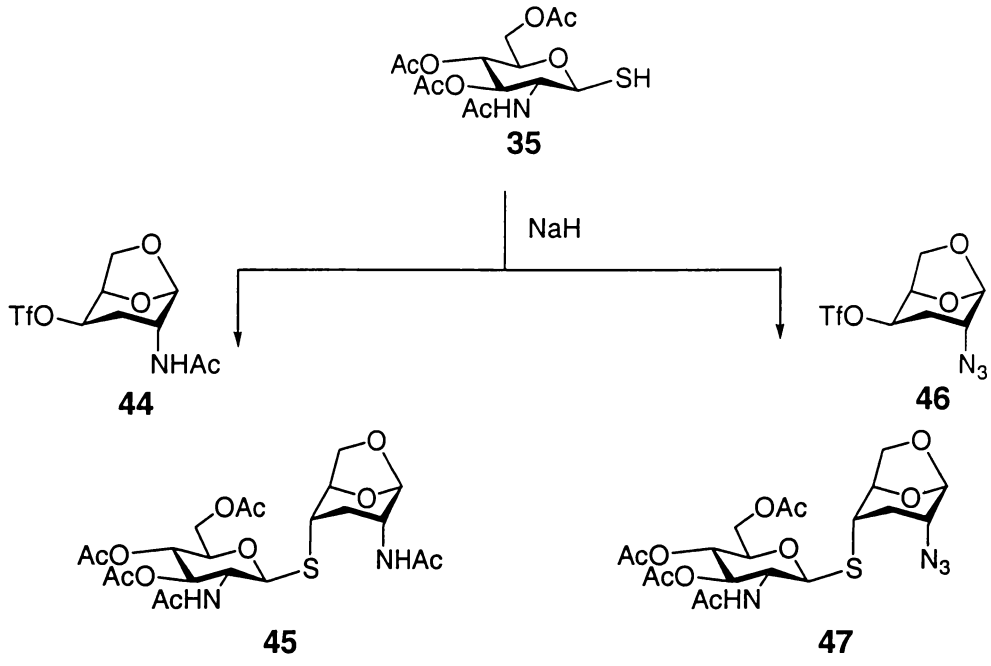


Scheme 9. Our Group's Previous Approach to *S*-linked Disaccharides (cont'd).



35 36 37 38 39 40 41 42 43

Scheme 10. Lee and Co-workers' Approach to an *S*-linked Tetrasaccharide.

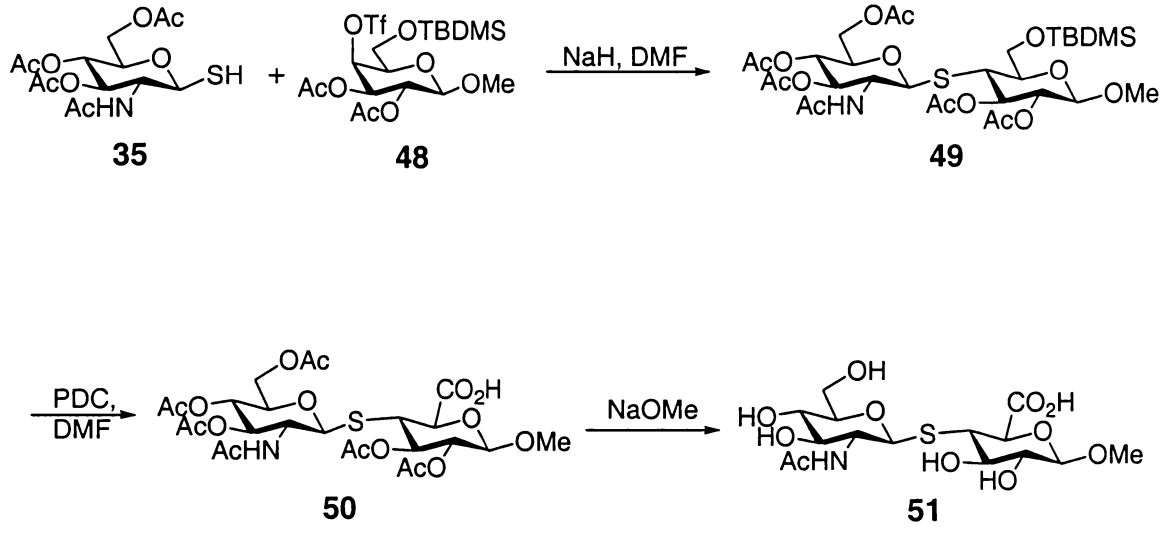


Scheme 11. Auzanneau and Co-workers' Approach to *S*-linked Disaccharides.

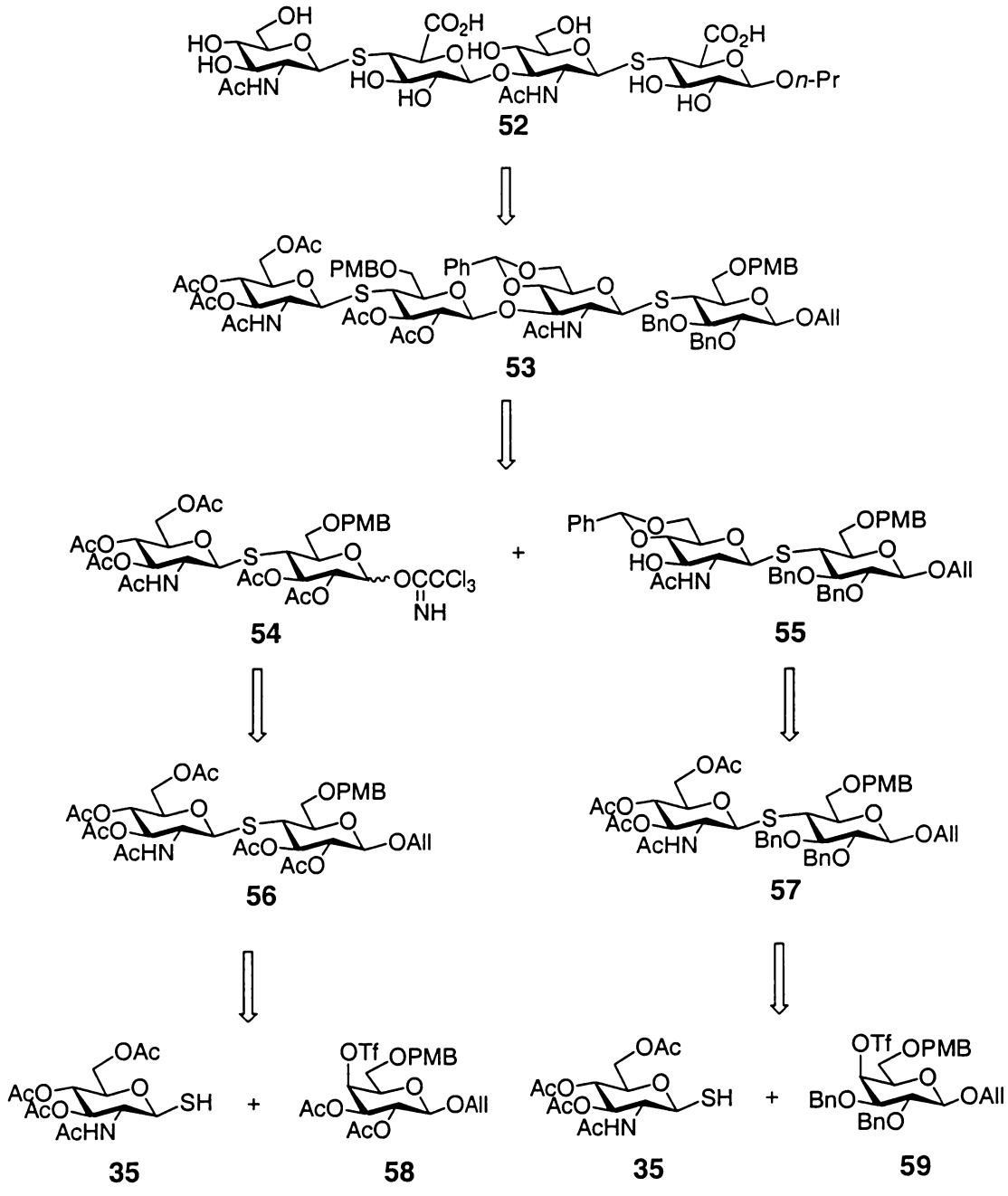
synthesis of higher order *S*-/*O*-linked HA oligosaccharide mimetics based on this disaccharide was not practical, and further efforts in the synthesis of higher order oligosaccharides failed (as shown in Scheme 12).

2.4.1. Retrosynthetic Analysis for *S*-/*O*-linked HA Tetrasaccharide Mimetics

Our immediate research goal was to synthesize *S*-/*O*-linked HA tetrasaccharide mimetics as it contains all the chemistry needed for the synthesis of higher order HA oligosaccharide mimetics, as well as provides us the material for NMR and molecular modeling studies, and for the study of the resistance to degradation by HA-degrading enzymes. If this is successful, efforts would be focused on the synthesis of higher order *S*-/*O*-linked HA oligosaccharide mimetics. A retrosynthetic analysis for the synthesis of *S*-/*O*-linked "mixed" tetrasaccharide **52** is shown in Scheme 13. The tetrasaccharide will be built up via Schmidt's trichloroacetimidate glycosylation. Two *S*-linked disaccharides building blocks, namely **56** and **57**, are proposed. The protective groups are strategically set up to allow: (a) upon deallylation and activation of compound **56** as trichloroacetimidate, compound **54** would serve as donor. An acetyl group was used on C-2 of the GlcA component to facilitate the formation of the β isomer in the coupling reaction; (b) after deacetylation and regioselective protection of compound **57**, the resulting compound **55** would serve as an acceptor, which is made possible by using benzyl groups as protective groups on the GlcA component. Furthermore, the GlcA moiety is protected to allow selective 6-deprotection-oxidation to the glucuronic acid (6–CO_2H group) at a late stage in the synthesis. Further disconnections go to the 1,4-thiol



Scheme 12. Our Group's Previous Approach to *S*-linked Disaccharides (cont'd).

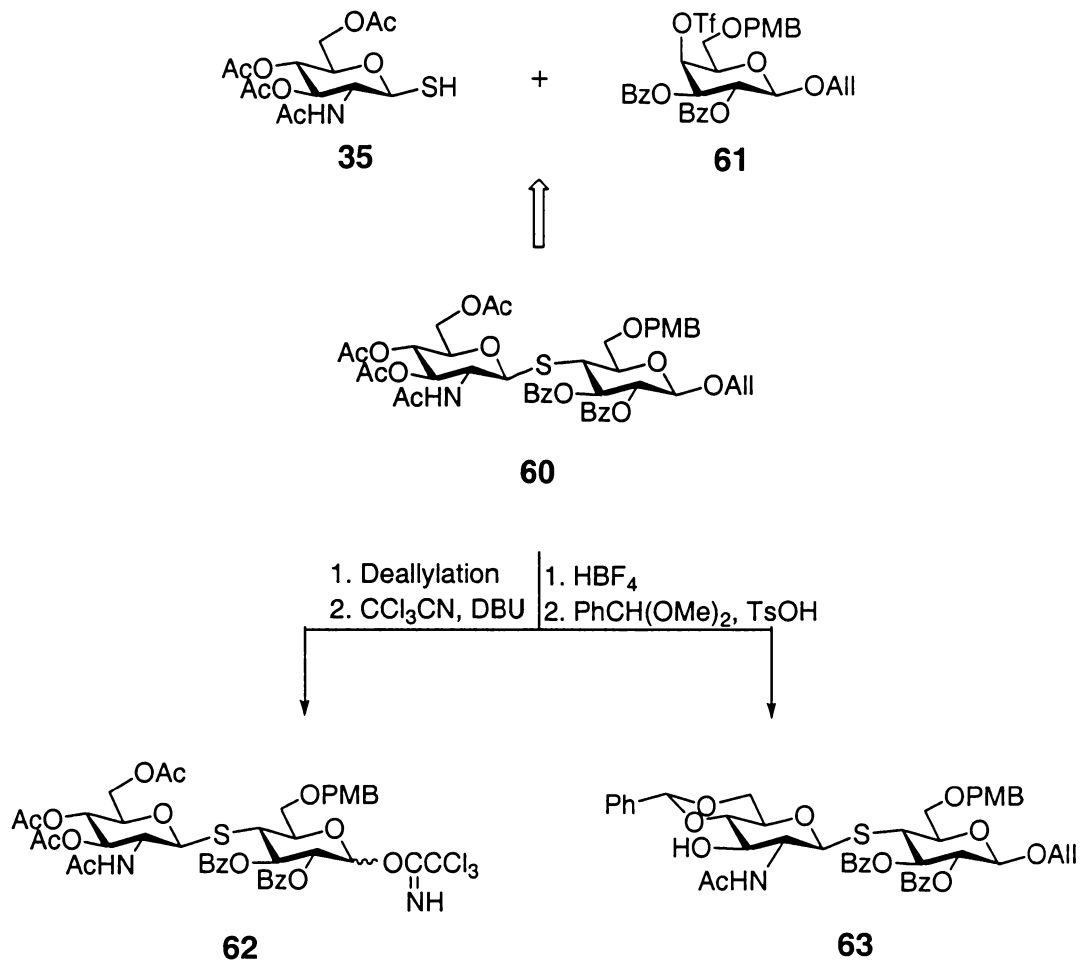


Scheme 13. Retrosynthetic Analysis of *S*-/*O*-linked Tetrasaccharide Mimetics.

bonds. Three key monosaccharides, **35**, **58**, and **59** are thus proposed.

2.4.2. Retrosynthetic Analysis for Higher Order *S*-/*O*-linked HA Oligosaccharide Mimetics

To satisfy the need for the synthesis of higher order *S*-/*O*-linked HA oligosaccharide mimetics, the protective groups for a universal *S*-disaccharide must meet the following requirements: (1) the protective group for the anomeric position could be selectively unveiled to allow activation to glycosyl donor, for example, trichloroacetimidate; (2) the glycosyl acceptor site must be protected to allow selective unmasking; (3) the GlcA moiety is protected to allow selective 6-deprotection-oxidation to the glucuronic acid (6–CO_2H group) at a late stage in the synthesis; and (4) all hydroxyl groups not involved in glycosylations must be permanently protected until final deprotection. Furthermore, an ester protective group should be considered for the C-2 position of the GlcA residue to facilitate the formation of the β isomer in the glycosylation reaction. Based on these requirements, two universal *S*-disaccharide building blocks were targeted. Methodology described by Yuan C. Lee and coworkers[73] will be employed in the formation of both disaccharides. In disaccharide **60**, benzoyl groups were chosen to protect the C-2 and C-3 positions of the GlcA residue since, according to Vince Pozsgay,[75] acetyl groups could be selectively unmasked in the presence of benzoyl groups. This gave us the possibility to synthesize acceptor **63** from disaccharide **60** by selective deacetylation and subsequent 4-,6-protection (as shown in Scheme 14). The second disaccharide **64** requires modification of the protective groups

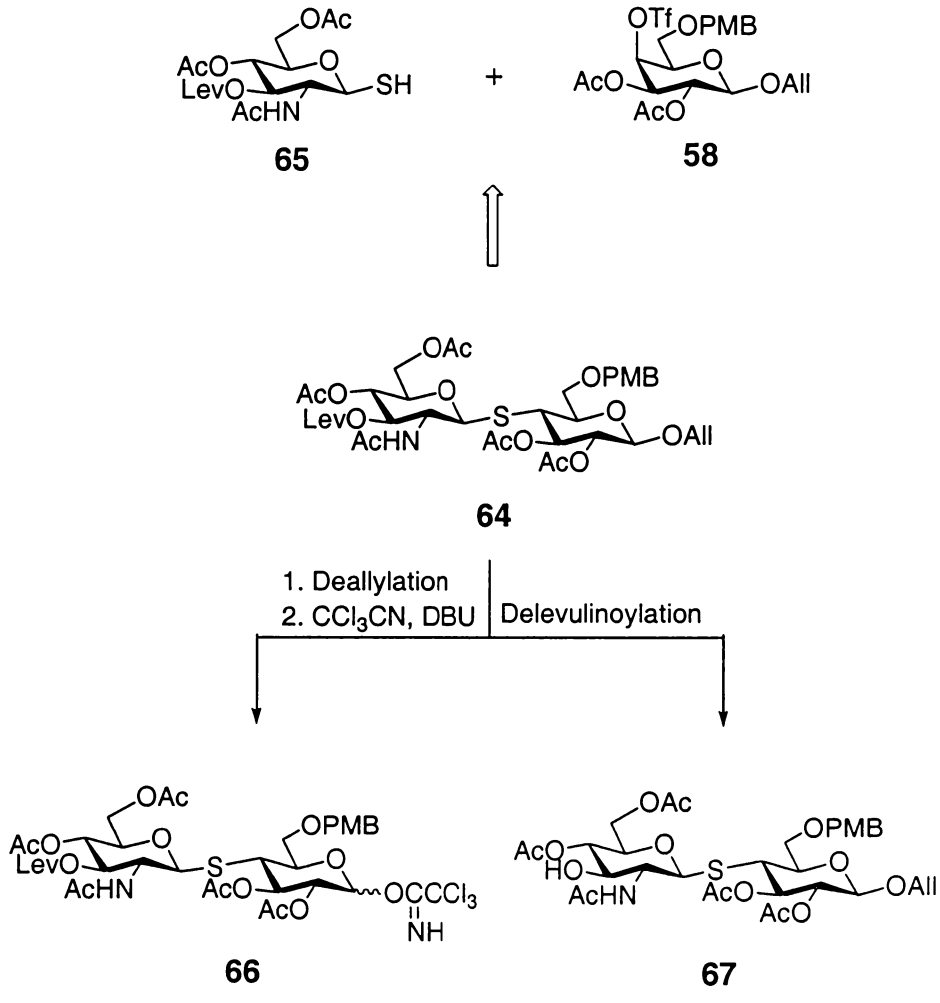


Scheme 14. Design of a Universal *S*-linked Disaccharide Building Block (Plan A).

on the GlcNAc residue. A levulinoyl group will be installed to protect the C-3 position since it could be selectively unveiled in the presence of acetyl groups.[76] In addition, all the protective groups could be unmasked with sodium methoxide or lithium hydroxide in the final deprotection. Although this GlcNAc residue is slightly different from the thiol **35** we proposed above, the chemistry involved would be totally different (as shown in Scheme 15).

2.5. Significance

The chemistry described in this dissertation is novel and refreshing. With respect to synthesis of *C*-/*O*-linked HA tetrasaccharide mimetics, very few examples exist in the literature. Although a *C*-linked disaccharide mimetic related to HA has been successfully obtained by our previous group member, this chemistry is limited in that it cannot be employed in the synthesis of higher order *C*-/*O*-linked HA oligosaccharide mimetics as manipulation of protective groups is impossible due to the severe reaction conditions employed. Additionally, generation of the requisite β stereochemistry is also a big issue. Compared to the synthesis of *C*-/*O*-linked compounds, synthesis of *S*-/*O*-linked HA oligosaccharide mimetics seems to be less complex, as this chemistry is well documented in the literature. However, sulfur might present problems in this particular case, since most oxidizing agents that oxidize hydroxyl groups to carboxylic acids also oxidize sulfur. Installation of the carboxylic acid group before coupling narrows down the coupling possibilities due to electronic effects. In addition, sulfur restrains the choice of protective groups as it poisons some transition metal catalysts (i.e., Pd/C).



Scheme 15. Design of a Universal *S*-linked Disaccharide Building Block (Plan B).

III. RESULTS AND DISCUSSION

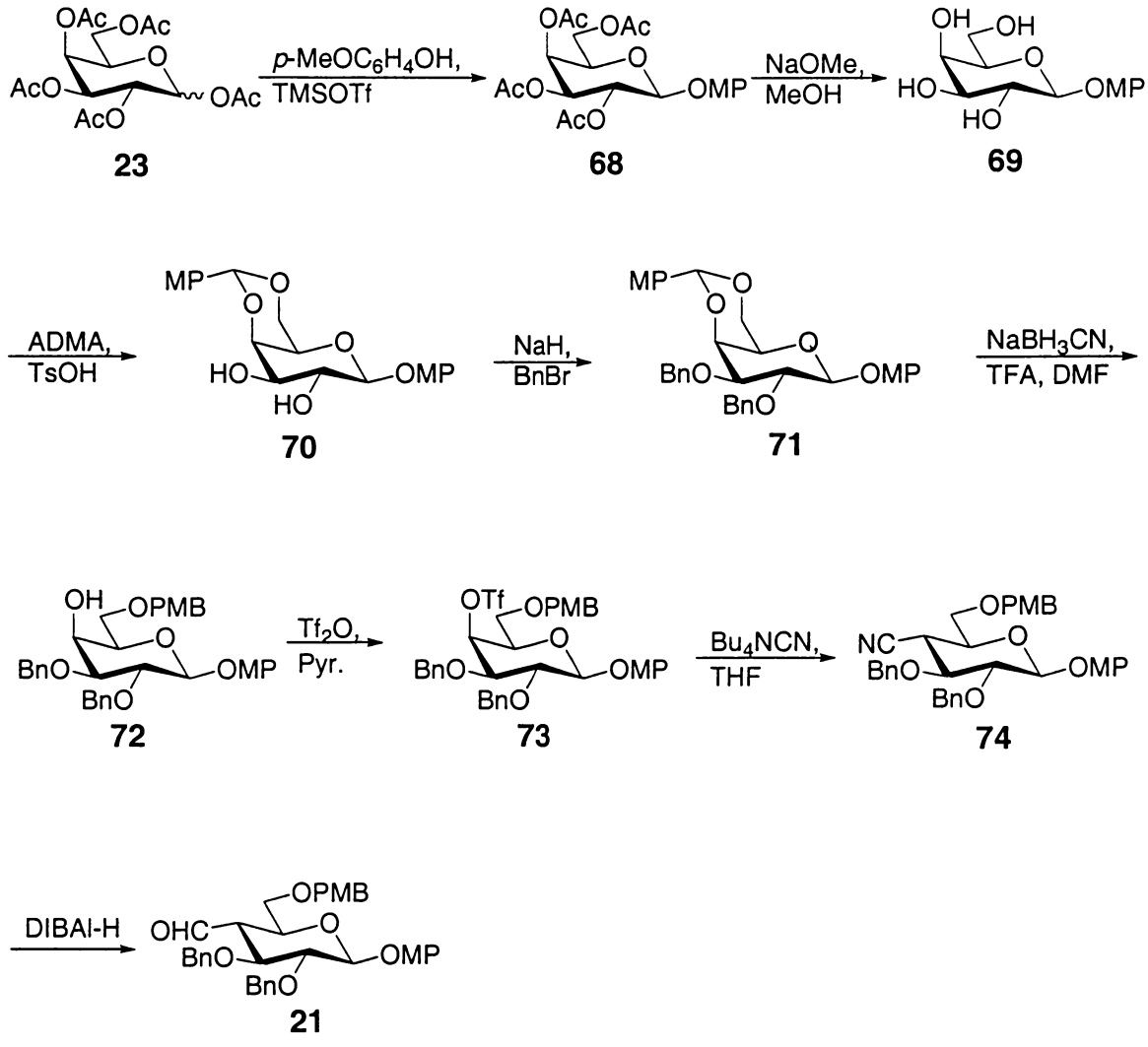
3. 1. Synthesis of *C*-/*O*-linked HA Tetrasaccharide Mimetics

As predicted in section 2.3, the SmI_2-promoted coupling reaction gave the desired disaccharides. However, condensation of the glycosyl donor and acceptor derived from disaccharide **19** gave predominantly the α tetrasaccharide. In order to facilitate the formation of the β tetrasaccharide, an acetyl group was required to be installed on C-2 of the glycosyl donor. While modification of protective groups of disaccharide **19** has proved to be time-consuming, as the synthesis of this disaccharide has already taken so many steps, an alternative glycosyl donor, trichloroacetimidate **91**, was synthesized according to the dianion method reported by Horst Kessler and co-workers. The synthesis of *C*-/*O*-linked HA tetrasaccharide mimetics has been accomplished by my co-worker, Dr. Zhong-Xu Ren, via condensation of trichloroacetimidate **91** and acceptor **84**, as detailed below.

3.1.1. Synthesis of Glycosyl Acceptor 84

3.1.1.1. Synthesis of GlcA Component 21

The synthesis of aldehyde **21** followed the 8-step procedure described in Kenneth Price's dissertation[66] as shown in Scheme 16. Hence, treatment of commercially available D-galactose pentaacetate **23** with *p*-methoxyphenol in dichloromethane (CH_2Cl_2) in the presence of trimethylsilyl trifluromethanesulfonate (TMSOTf) at 0 °C for 3 h afforded only the desired β-anomer **68**, as confirmed by ^{1}HNMR spectroscopy with a coupling

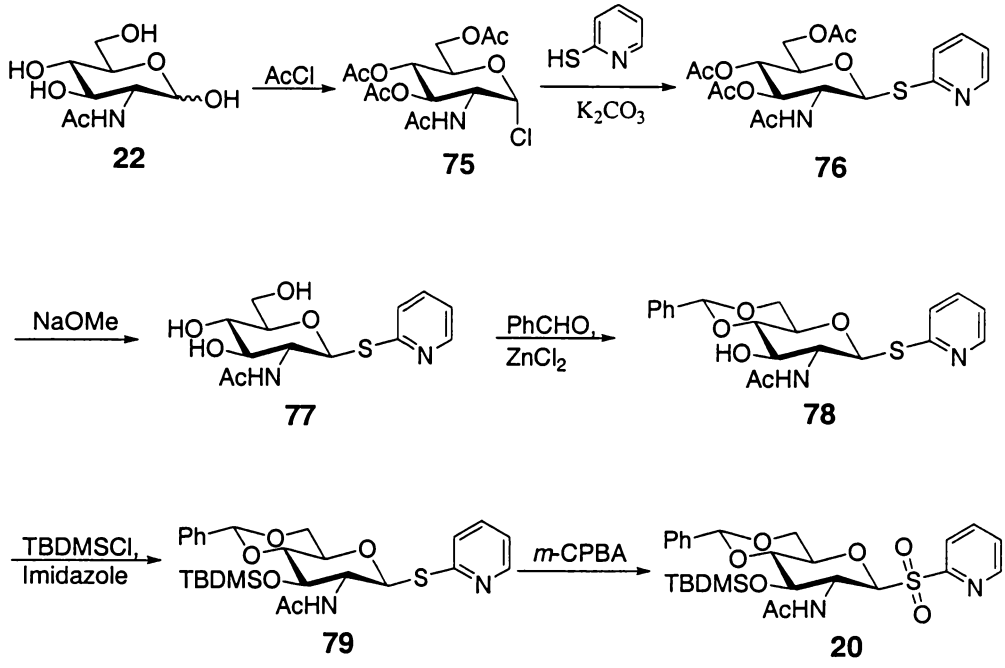


Scheme 16. Synthesis of GlcA Component 21.

constant of $J_{H1, H2}$ = 10.8 Hz.[77] Deacetylation of **68** with sodium methoxide (NaOMe) in 1:5 dichloromethane (CH_2Cl_2) and methanol gave the corresponding tetraol **69** in nearly quantitative yield. Regioselective bis-protection of the 4-OH and 6-OH positions with a *p*-methoxybenzylidene group was accomplished via treatment of tetraol **69** with anisaldehyde dimethyl acetal (ADMA) in the presence of a catalytic amount of *p*-toluenesulfonic acid (TsOH) in dry acetonitrile to afford diol **70** as a precipitate in 84% yield.[78] The resulting diol **70** was then treated with sodium hydride (NaH) at 0 °C for 10 min, followed by addition of benzyl bromide (BnBr) in *N*,*N*-dimethylformamide (DMF), to give compound **71** in 95% yield. Regioselective reductive cleavage of the benzylidene ring of compound **71** was achieved via treatment with sodium cyanoborohydride ($NaBH_3CN$) and trifluroacetic acid (TFA) in the presence of 4 Å MS in *N*,*N*-dimethylformamide (DMF) at r. t. for 10 h to render the 4-OH isomer **72** in 74% yield as the major product, along with the 6-OH isomer as a byproduct (21%).[79] Treatment of compound **72** with trifluoromethanesulfonic anhydride (Tf_2O) in pyridine at 0 °C overnight gave the corresponding triflate **73** in nearly quantitative yield. Exposure of triflate **73** to tetrabutylammonium cyanide (Bu_4NCN) in tetrahydrofuran (THF) afforded the S_N2 substitution product **74** in 60% yield. The main byproduct was presumably the E2 elimination product, which is slightly less polar than the substitution product on TLC. Reduction of compound **74** with diisobutylaluminum hydride (DIBAl-H) in tetrahydrofuran (THF) at –78 °C, followed by treatment with 1.0 N phosphoric acid (H_3PO_4) at 0 °C, afforded aldehyde **21** in 71% yield.[66,80,81]

3.1.1.2. Synthesis of GlcNAc Component 20

The synthesis of GlcNAc component **20** was carried out as shown in Scheme 17. Hence, treatment of commercially available 2-acetamido-2-deoxy-α-D-glucose (**22**) with acetyl chloride afforded 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**75**).[82] Exposure of chloride **75** to K_2CO_3 and 2-mercaptopyridine in dry acetone at r. t. gave the desired pyridinyl sulfide **76**. Only the β isomer was isolated in this reaction, as confirmed by ^{1}HNMR spectroscopy with a coupling constant of $J_{H1, H2} = 10.5$ Hz.[83] In order to manipulate the protective groups, sulfide **76** was treated with sodium methoxide (NaOMe) in 1:5 dichloromethane (CH_2Cl_2) and methanol to afford triol **77**. Then, a benzylidene ring was installed to mask the 4- and 6-positions via treatment with benzaldehyde and zinc chloride ($ZnCl_2$) at r. t. for 10 h.[84,85] A combination of benzaldehyde dimetyl acetal and *p*-toluenesulfonic acid (TsOH), which works in most cases, gave complicated results, due no doubt to the fact that *p*-toluenesulfonic acid (TsOH) reacts with the pyridinyl residue. Treatment of compound **78** with *tert*-butyldimethylsilyl chloride (TBDMSCl) in the presence of imidazole in *N*,*N*-dimethylformamide (DMF) at r. t. overnight gave compound **79**,[69] which was readily converted to the corresponding sulfone **20** in good yield (79%) via treatment with *m*-chloroperoxybenzoic acid (*m*-CPBA) and sodium carbonate (Na_2CO_3) in dichloromethane (CH_2Cl_2) at 0 °C. (compare with the yield (12%) reported by Beau and co-workers.[86])

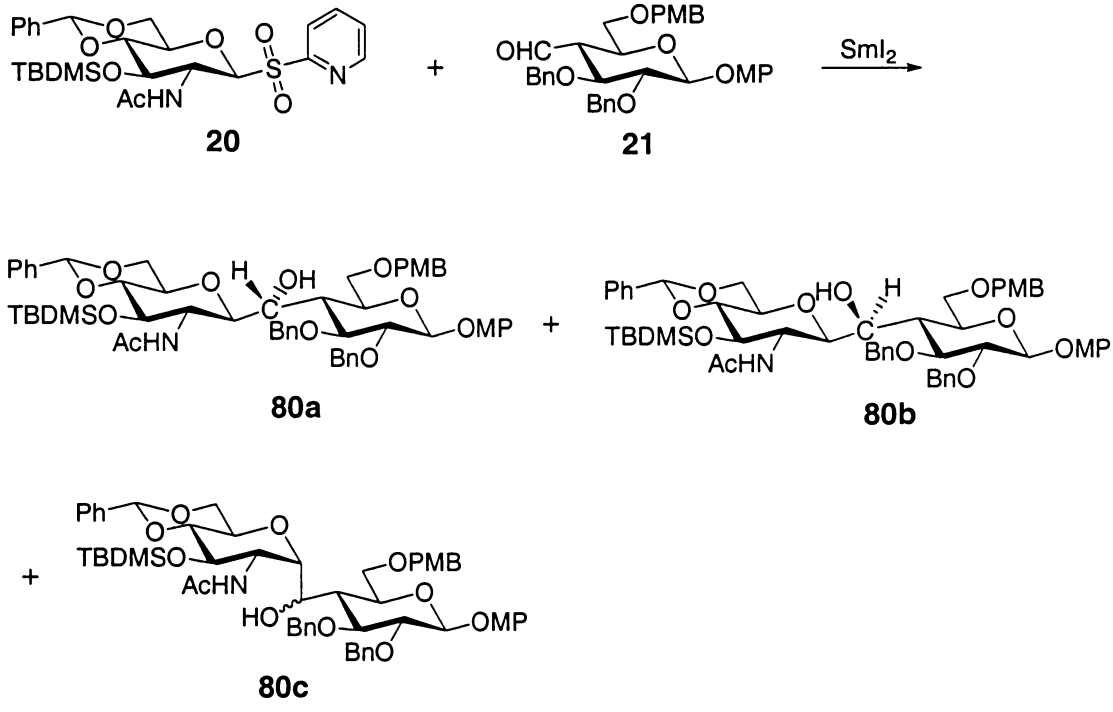


Scheme 17. Synthesis of GlcNAc Component 20.

3.1.1.3. Samarium Diiodide Promoted Coupling Reaction

With aldehyde **20** and sulfone **21** in hand, the stage was set for the synthesis of *C*-disaccharides. The coupling reaction was carried out under the promotion of samarium diiodide (SmI_2) in tetrahydrofuran (THF) at r. t. as planned. In this reaction, two chiral centers were involved, which would give four possible isomers. Actually, only one α isomer **80c** and two β isomers (**80a** and **80b**) were isolated. As a radical or anion intermediate was involved in this reaction, the selectivity of this reaction was predicted to be relatively poor; however, to our surprise, we found that the two β isomers were obtained as major products (as shown in Scheme 18). All the three disaccharides were easily identified by positive-ion mode ESIMS spectra (as shown in Figure 5-7). However, it is it extremely difficult to fully characterize these disaccharides as the signal of H-1′ in the 1D and 2D (gCOSY, HSQC) NMR spectra was obscured by several other signals (for spectra, refer to Appendix II).

Fortunately, the absolute structure of disaccharide **80a** was ascertained via X-ray crystallography as shown in Figure 8 and Figure 9 (for crystal data, refer to Appendix I). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexanes into a saturated solution of compound **80a** in ethyl acetate (EtOAc). Disaccharide **80b** was also shown to have the β linkage as, after deoxygenation, it gave the same disaccharide as that of **80a** (as described below), while disaccharide **80c** was assigned as the α anomer as the deoxygenated derivative of **80c** is different from that of **80a** and **80b**. Conversion of the α isomer **80c** to the β isomers (**80a** and **80b**) was achieved by my co-worker, Dr. Zhong-Xu Ren, via oxidation of compound **80c** to the corresponding α



Scheme 18. Samarium Diiodide Promoted Coupling Reaction.

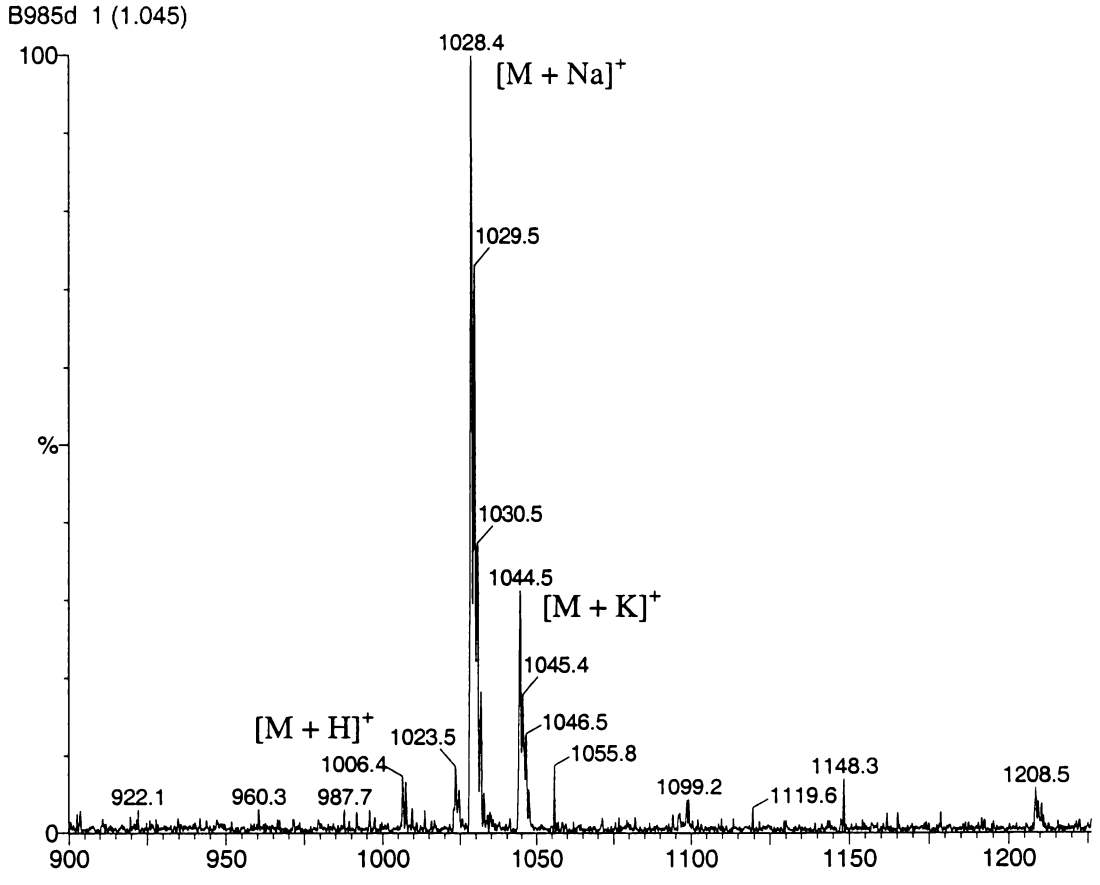


Figure 5. Positive-Ion Mode ESIMS of 80a.

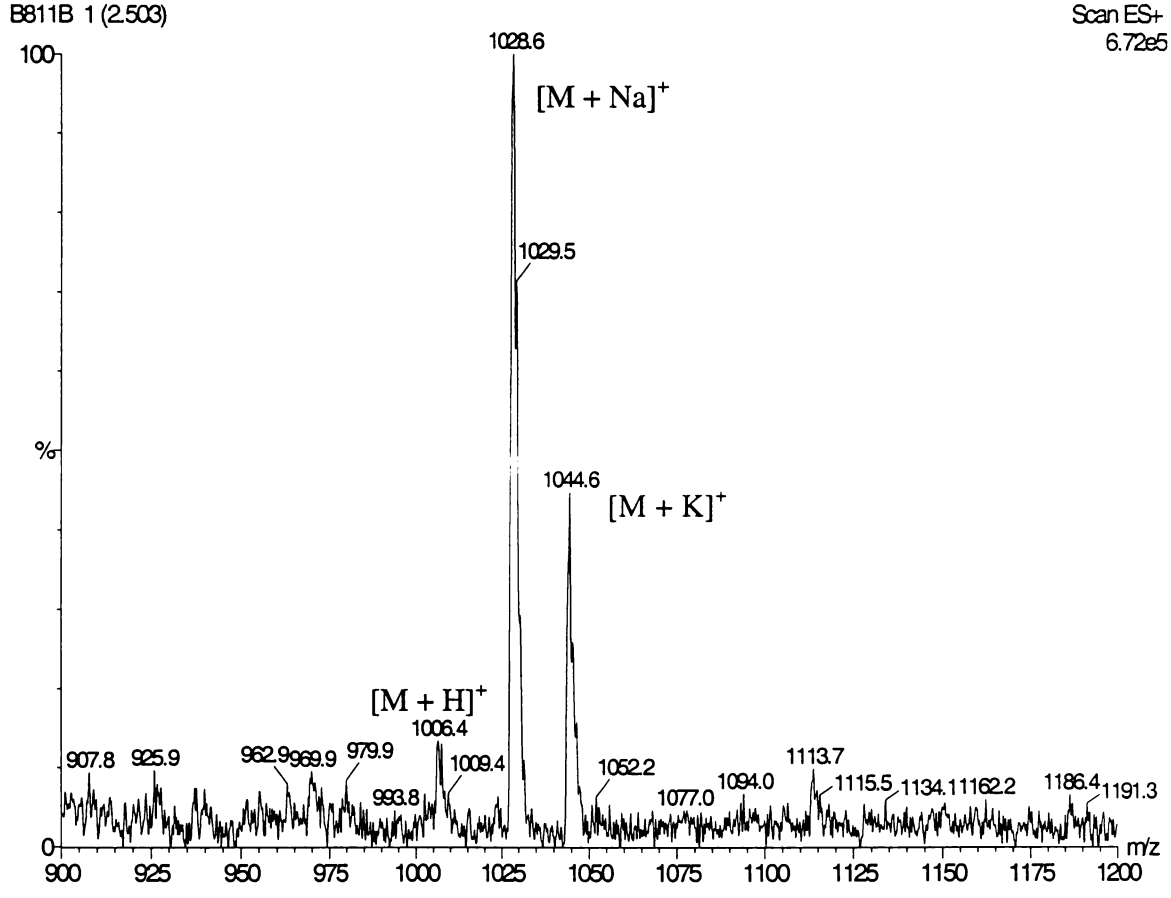


Figure 6. Positive-Ion Mode ESIMS of 80b.

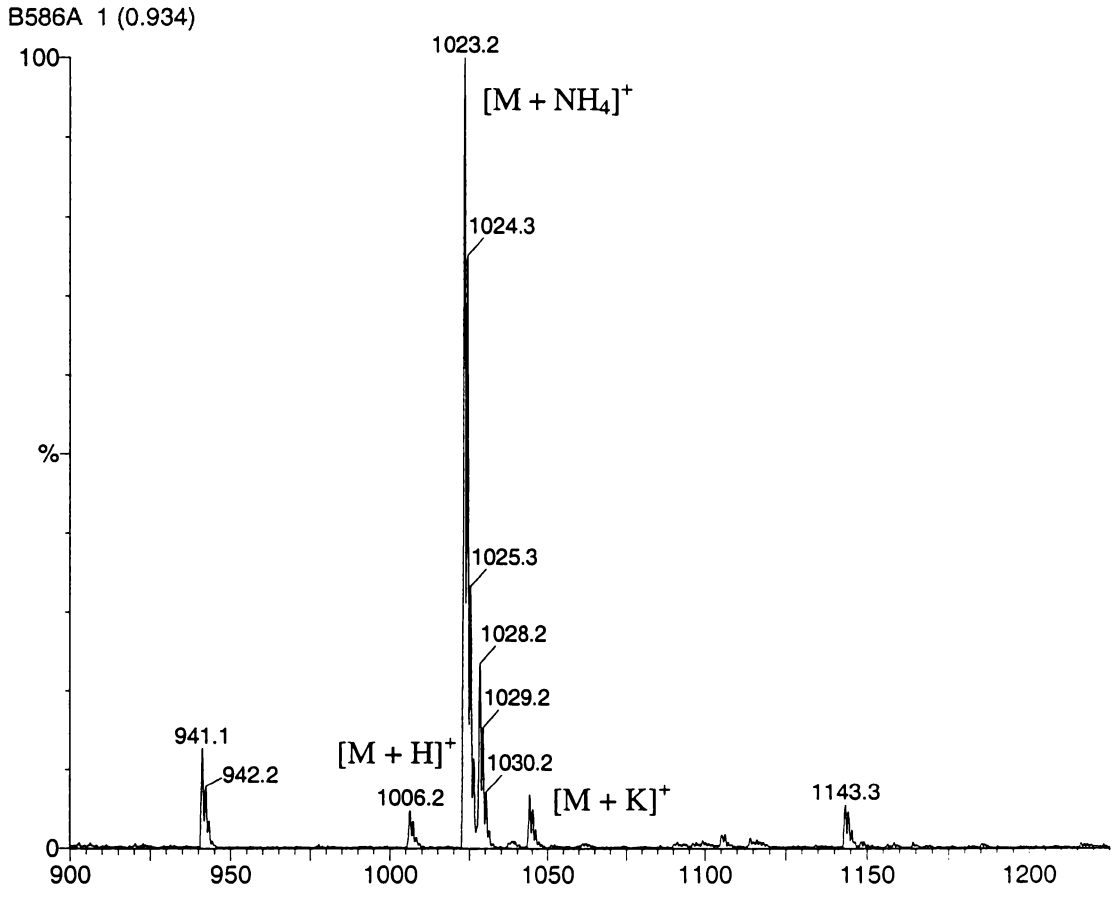


Figure 7. Positive-Ion Mode ESIMS of 80c.

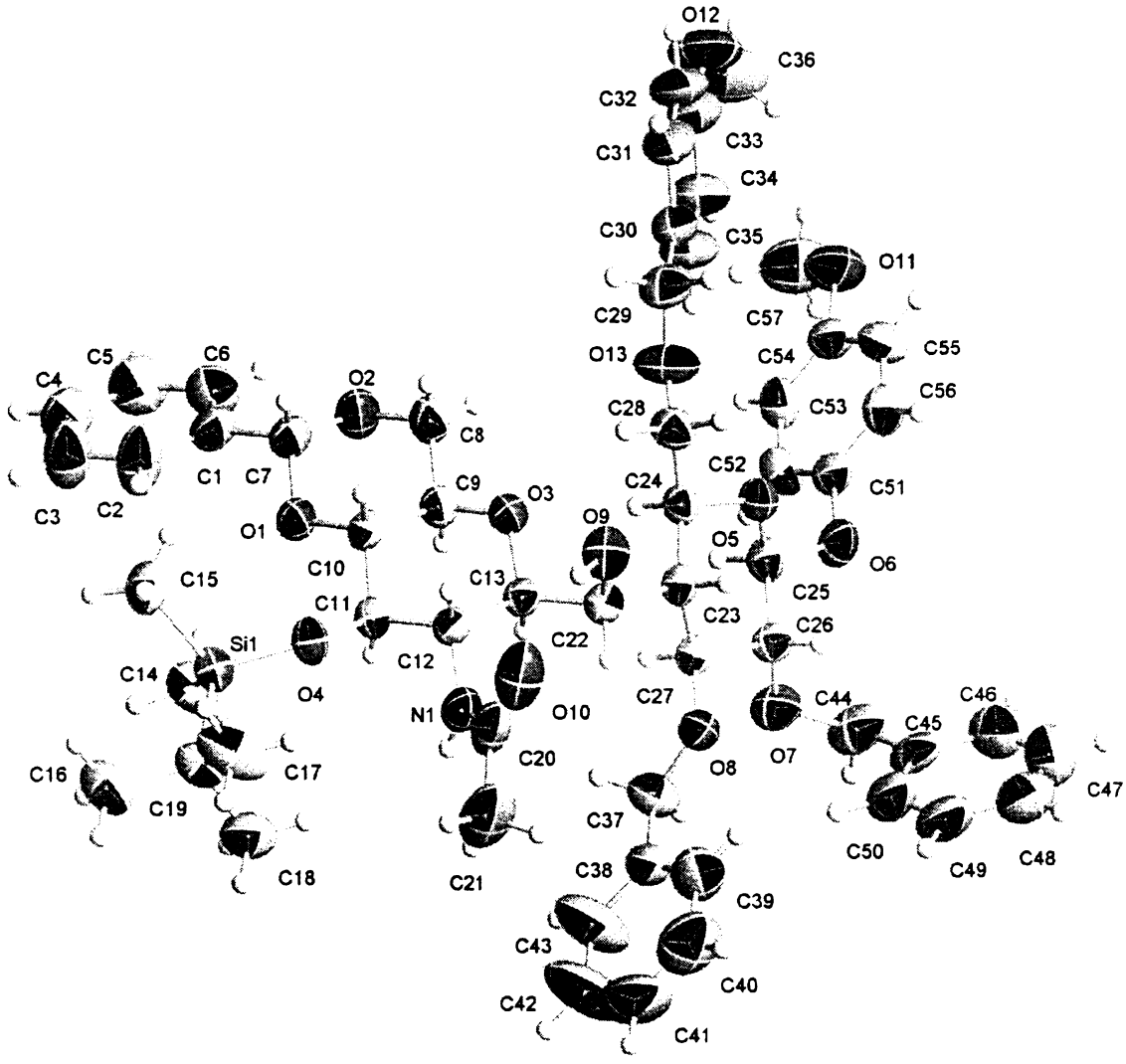


Figure 8. ORTEP of β Epimer 80a.

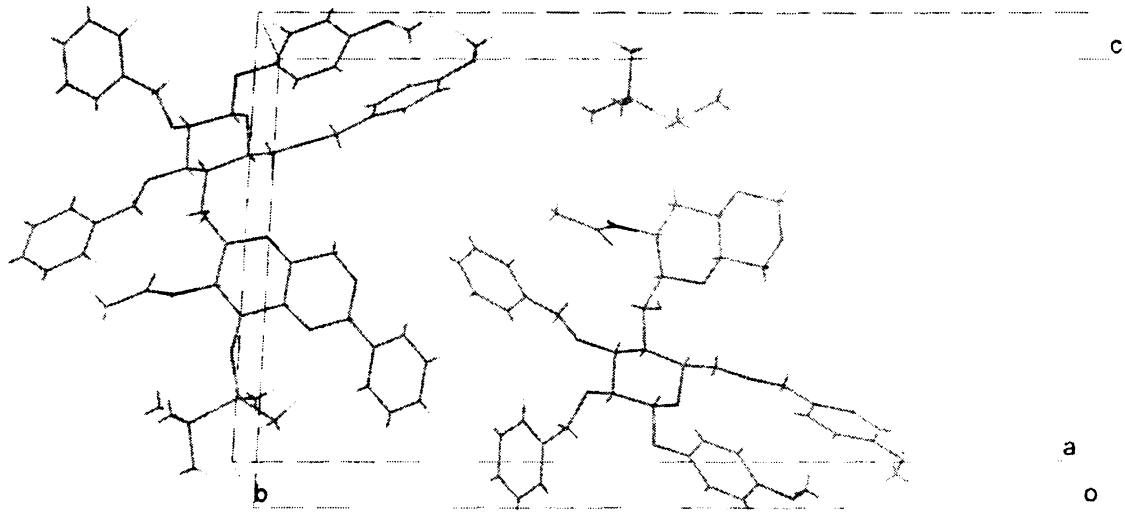


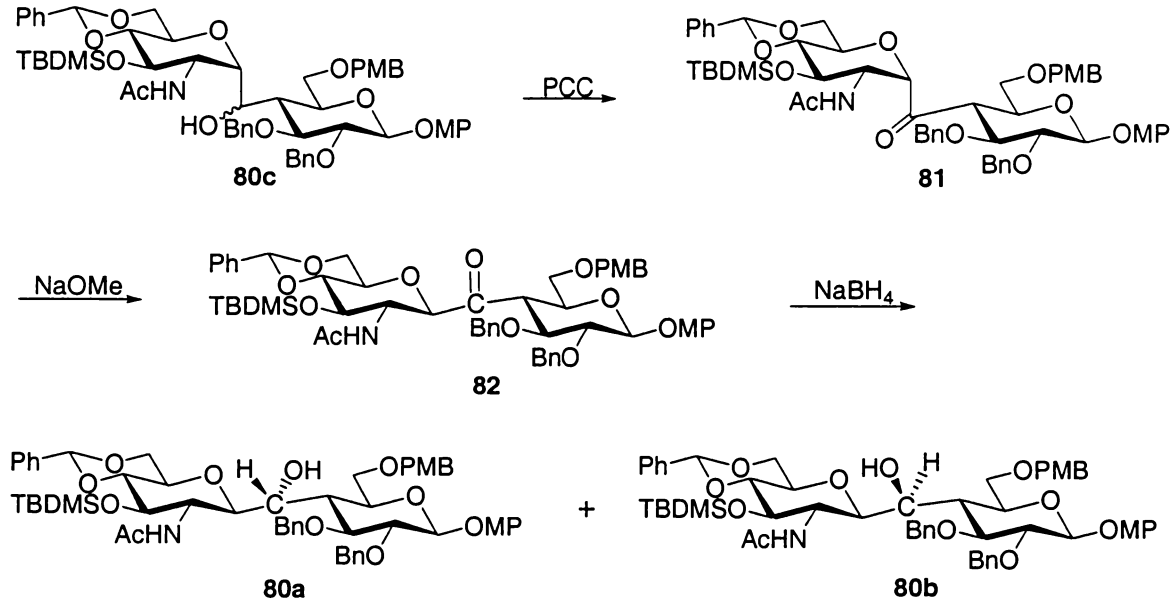
Figure 9. Crystal Pack of β Epimer 80a.

ketone **81** with pyridinium chlorochromate (PCC) in dichloromethane (CH_2Cl_2), isomerization of the resulting α ketone **81** to the β ketone **82** with sodium methoxide (NaOMe) in methanol, and subsequent reduction of the β ketone **82** to **80a** and **80b** with sodium borohydride ($NaBH_4$) in ethanol (EtOH) (as shown in Scheme 19). Removal of the hydroxyl moiety was achieved according to Barton and McCombie.[87,88] Thus treatment of **80a** or **80b** with sodium hydride (NaH) in the presence of imidazole in tetrahydrofuran (THF), followed by addition of carbon disulfide (CS_2) and then methyl iodide (MeI) after 40 min, afforded **83a** or **83b** in 54% or 52% yield, respectively. Exposure of **83a** or **83b** to tri-*n*-butyltin hydride (*n*-Bu_3SnH) and azoisobutyronitrile (AIBN) in refluxing toluene afforded the desired disaccharide **19** in 91% yield, which after removal of the *tert*-butyldimethylsilyl (*O*-TBDMS) group with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF), gave acceptor **84** in 93% yield (as shown in Scheme 20).

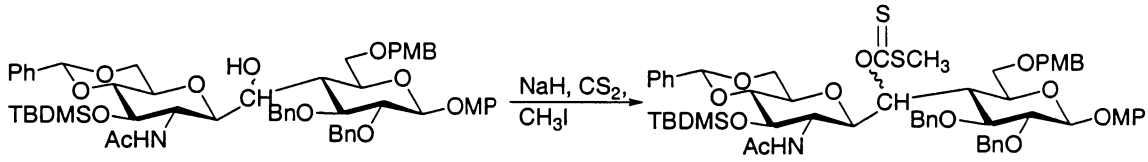
Acceptor **84** has been handed over to co-worker, Dr. Zhong-Xu Ren, for completion of the synthesis of *C*-/*O*-linked HA tetrasaccharide mimetics as follows.

3.1.2. Synthesis of Trichloroacetimidate 91

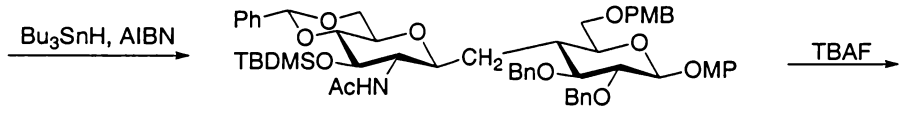
C-disaccharides **85a** and **85b** were prepared according to the method reported by Horst Kessler and co-workers as shown in Scheme 21.[60-62] Hence, deprotonation of compound **10** in tetrhydrofuran (THF) was achieved with methyllithium (MeLi) at –78 °C, followed by treatment with butyllithium (BuLi) at –60 °C, which provided a dianion intermediate (as indicated by a deep red color of the solution) that was reacted with



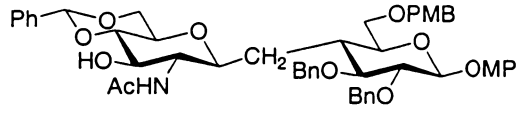
Scheme 19. Conversion of 80c to 80a and 80b.



80a or **80b** **83a** or **83b**

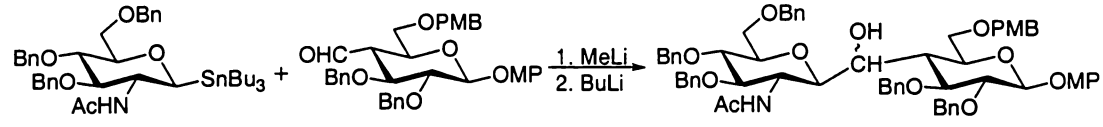


19

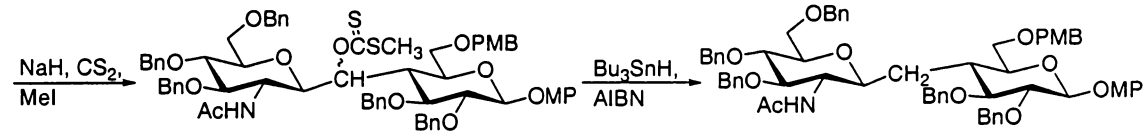


84

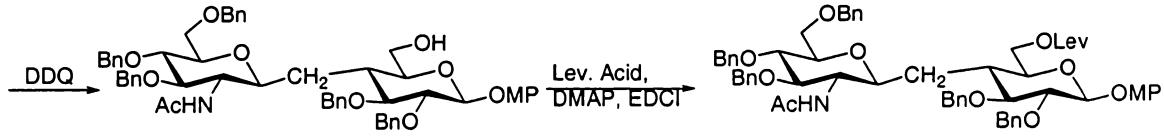
Scheme 20. Synthesis of Acceptor 84.



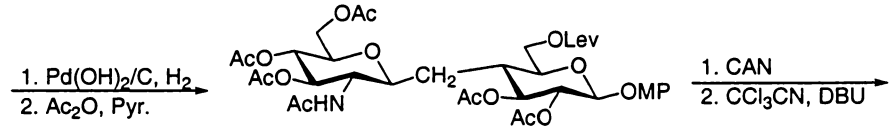
10 **21** **85a** and **85b**



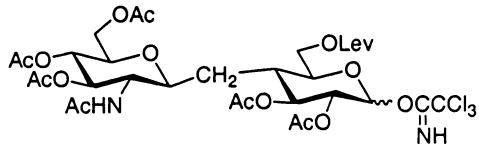
86a and **86b** **87**



88 **89**



90



91

Scheme 21. Synthesis of Trichloroacetimidate 91.

aldehyde **21** *in situ* to give disaccharides **85a** and **85b** in 31% and 28% yield respectively. Only the two desired β isomers **85a** and **85b** were isolated in this reaction, as confirmed by 1D and 2D NMR spectra (gCOSY, HSQC). Treatment of **85a** or **85b** with sodium hydride (NaH) in the presence of imidazole in dry tetrahydrofuran (THF), followed by addition of carbon disulfide (CS_2), and then methyl iodide (MeI) after 40 min, afforded xanthogenate **86a** or **86b** in 81% or 80% yield, respectively, which upon treatment with tri-*n*-butyltin hydride (*n*-Bu_3SnH) in the presence of azoisobutyronitrile (AIBN) in refluxing toluene, gave the desired deoxygenated derivative **87** in 66% yield. In order to facilitate the formation of the β-(1→3)-linked tetrasaccharide using trichloroacetimidate glycosylation, the protective groups on disaccharide **87** were modified as follows. Removal of the *p*-methoxybenzyl (PMB) group was achieved via treatment of disaccharide **87** with 2,3-dichloro-5,6-dicyano-1,4 benzoquinone (DDQ) in 15:1 dichloromethane (CH_2Cl_2) and water at r. t. for 1.5 h to afford disaccharide **88** in 95% yield,[89] which upon levulinoylation with levulinic acid and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDCI) in dichloromethane (CH_2Cl_2) in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP),[90] afforded disaccharide **89** in nearly quantitative yield. Treatment of disaccharide **89** with Pearlman's catalyst, $Pd(OH)_2/C$, in a hydrogen (H_2) atmosphere at r. t. for 3 days, followed by acetylation with acetic anhydride (Ac_2O) in pyridine at r. t. overnight, gave compound **90** in 80% yield. Removal of the *p*-methoxyphenyl (MP) group on the anomeric carbon with ammonium cerium(IV) nitrate (CAN) in 4:1 acetonitrile and water (84% yield, with an α, β anomeric ratio of 6:1), followed by treatment of the resulting disaccharide with trichloroacetonitrile

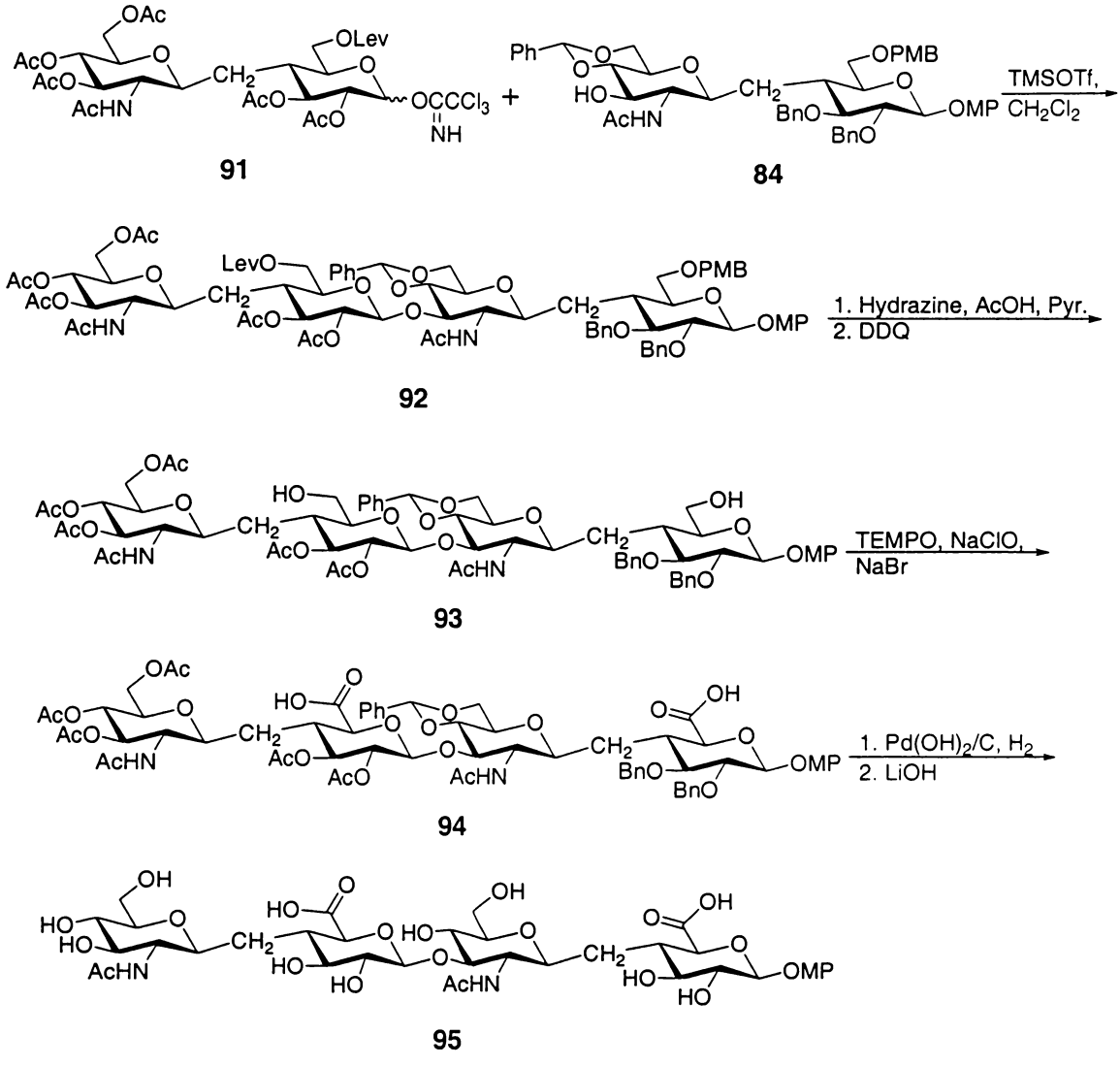
(CCl_3CN) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane (CH_2Cl_2) at r. t. for 1 h, gave the desired trichloroacetimidate **91** in 79% yield, , with an α, β anomeric ratio of 2.4:1.[91]

3.1.3. Synthesis of *C*-/*O*-linked HA Tetrasaccharide Mimetics

Condensation of trichloroacetimidate **91** and acceptor **84** was achieved via treatment with a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in dichloromethane (CH_2Cl_2) at –15 °C for 2 h to afford the protected tetrasaccharide **92** in 56% yield.[92] Removal of the levulinoyl (Lev) group with hydrazine in the presence of acetic acid (AcOH) in pyridine at r. t., followed by removal of *p*-methoxybenzyl (PMB) group with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 15:1 dichloromethane (CH_2Cl_2) and water at r. t., afforded diol **93** in 41% yield. Oxidation of the resulting diol **93** to the corresponding carboxylic acid **94** was achieved in 57% yield via treatment with 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and aq NaOCl in the presence of a catalytic amount of sodium bromide (NaBr).[93] Finally, debenzylation with Pearlman's catalyst, $Pd(OH)_2/C$, in a hydrogen (H_2) atmosphere in ethyl acetate (EtOAc) and methanol (MeOH) for 3 days, followed by deacetylation with lithium hydroxide (LiOH) in 1:2 tetrahydrofuran (THF) and water at r. t. for 10 h, furnished the target tetrasaccharide **95** in 72% yield (as shown in Scheme 22).

3.2. Synthesis of *S*-/*O*-linked HA Tetrasaccharide Mimetics

Although the introduction and presence of sulfur functionality presented problems

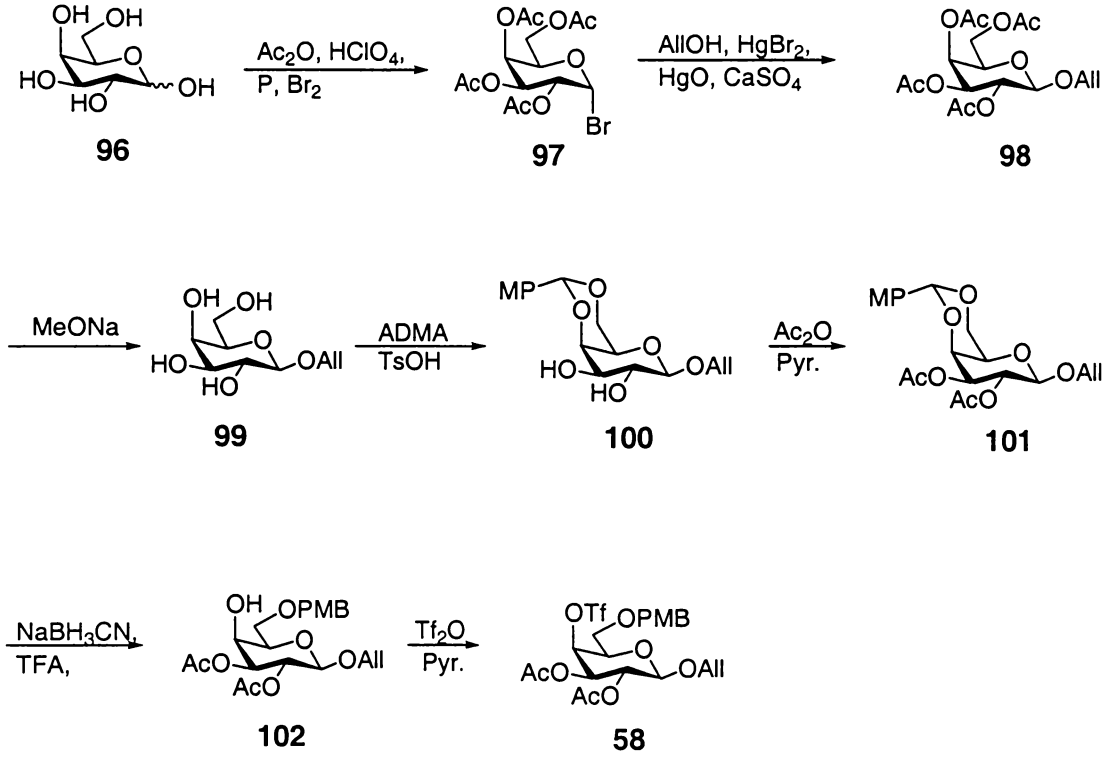


Scheme 22. Synthesis of *C*-/*O*-linked HA Tetrasaccharide Mimetics.

in oxidation and debenzylation as predicted in section 2.5, the synthesis of *S*-/*O*-linked HA tetrasaccharide mimetics went exactly as planed as detailed below.

3.2.1. Synthesis of Trichloroacetimidate 54

Triflate **58** required for the synthesis of *S*-disaccharide **56** was prepared by following a 7-step procedure beginning with commercially available compound, D-galactose (**96**) as shown in Scheme 23. Hence, treatment of compound **96** with acetic anhydride (Ac_2O) in the presence of perchloric acid ($HClO_4$), followed by addition of red phosphorus (P) and bromine (Br_2), afforded glycosyl bromide **97**. Glycosylation with allyl alcohol was achieved in chloroform ($CHCl_3$) under the promotion of mercuric bromide ($HgBr_2$) and mercuric oxide (HgO) in the presence of calcium sulfate anhydride ($CaSO_4$) to give compound **98** in nearly quantitative yield.[94] After deacetylation with sodium methoxide (NaOMe) in 1:5 dichloromethane (CH_2Cl_2) and methanol (MeOH), the resulting tetraol **99** was treated with anisaldehyde dimethyl acetal (ADMA) in the presence of a catalytic amount of *p*-toluenesulfonic acid (TsOH) in dry acetonitrile (CH_3CN) at r. t. for 2 h to give regioselectively protected compound **100** with the 4- and 6-positions protected with a *p*-methoxybenzylidene group, which precipitated out in 88% yield. Acetylation of diol **100** was achieved via treatment with acetic anhydride (Ac_2O) in pyridine at r. t. to give compound **101** in 91% yield. Regioselective reductive cleavage of the benzylidene ring to a free 4-OH and a 6-*O*-*p*-methoxybenzyl (PMB) ether (compound **102**) was effected with sodium cyanoborohydride ($NaBH_3CN$) and trifluoroacetic acid (TFA) in the presence of 4 Å MS in 91% yield, along with a trace of the 6-OH isomer as

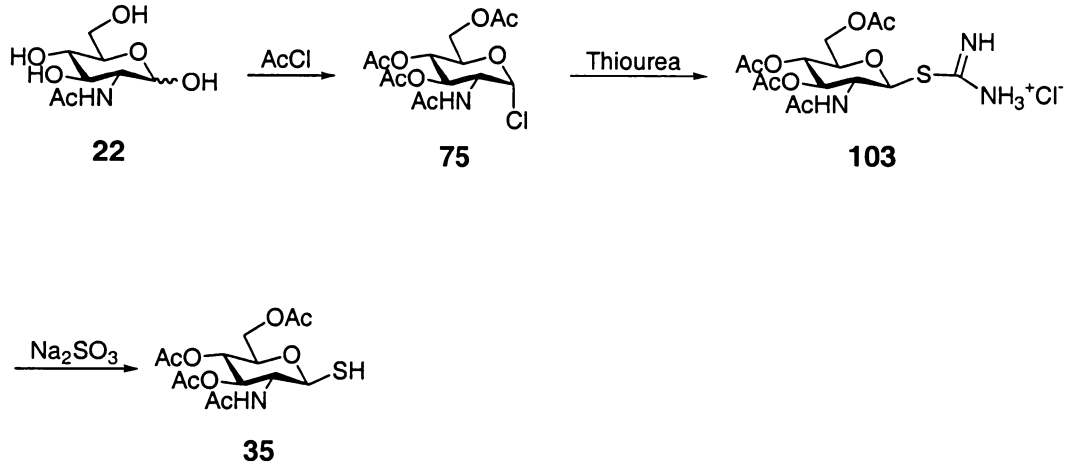


Scheme 23. Synthesis of Triflate 58.

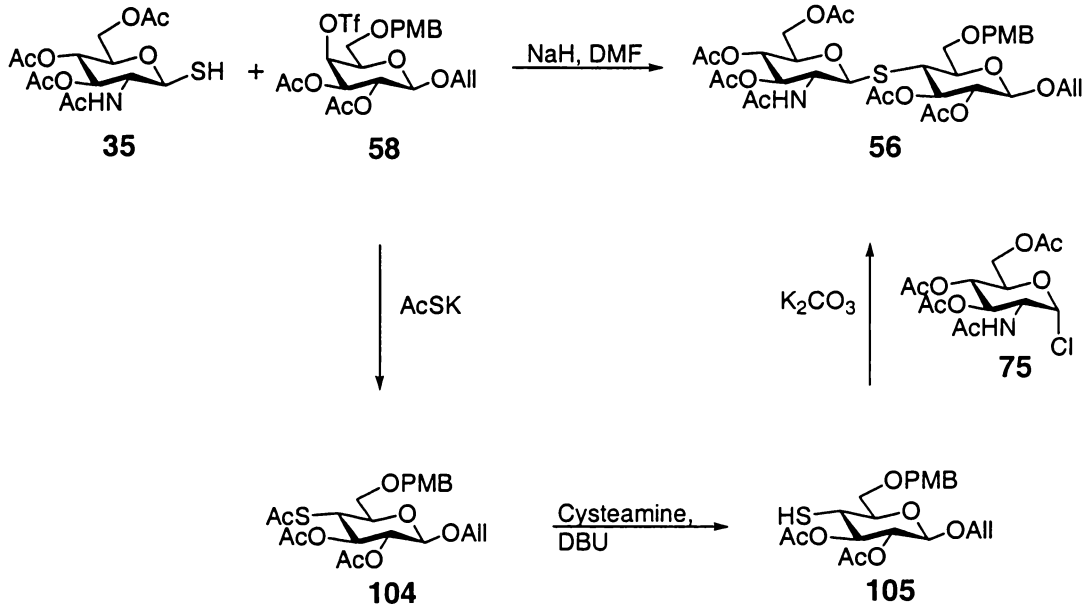
a byproduct.[95] Upon activation of the hydroxyl group as the triflate derivative with triflic anhydride (Tf_2O) in pyridine at 0 °C overnight, triflate **58** was synthesized in nearly quantitative yield.

Synthesis of thiol **35** proceeded from commercially available compound, 2-acetiamido-2-deoxy-D-glucose (**22**) as shown in Scheme 24, According to Horton and Wolfrom,[96] following treatment of compound **22** with acetyl chloride (AcCl) at r. t. overnight, the glycosyl chloride **75** thus obtained was exposed to thiourea in refluxing acetone to give pseduthiourea derivative **103** as a precipitate, which was readily converted to thiol **35** in nearly quantitative yield via treatment with sodium sulfite (Na_2SO_3) in 5:1 water and acetone at r. t. for 2 h.[97]

Base-promoted coupling of thiol **35** and triflate **58** was carried out in *N*,*N*-dimethylformamide (DMF) at 0 °C via treatment of thiol **35** with sodium hydride (NaH) for 10 min, followed by addition of triflate **58**, to give the desired *S*-linked disaccharide **56** in 51% yield. However, this reaction suffered from low yield due to the fact that sodium hydride (NaH) is a strong base, which partially deprotected the acetyl groups in the coupling reaction. In order to improve the yield of disaccharide **56**, an alternative route, has been developed, albeit via the less common "reverse strategy" of reacting a 4–SH glycosyl acceptor with a suitably activated glycosyl donor, namely, glycosyl chloride **75**, as shown in Scheme 25. Hence, treatment of triflate **58** with potassium thioacetate (KSAc) in *N*,*N*-dimethylformamide (DMF) at 0 °C afforded thioacetate **104** in 76% yield.[98] Subsequent *S*-deacetylation of thioacetate **104** with cysteamine in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in *N*,*N*-dimethylformamide



Scheme 24. Synthesis of Thiol 35.

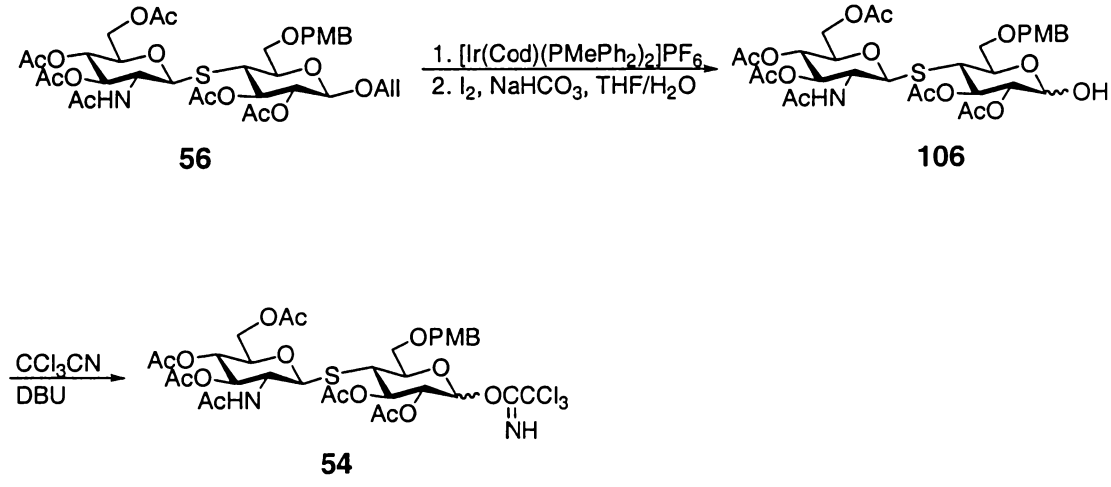


Scheme 25. Synthesis of *S*-linked Disaccharide 56.

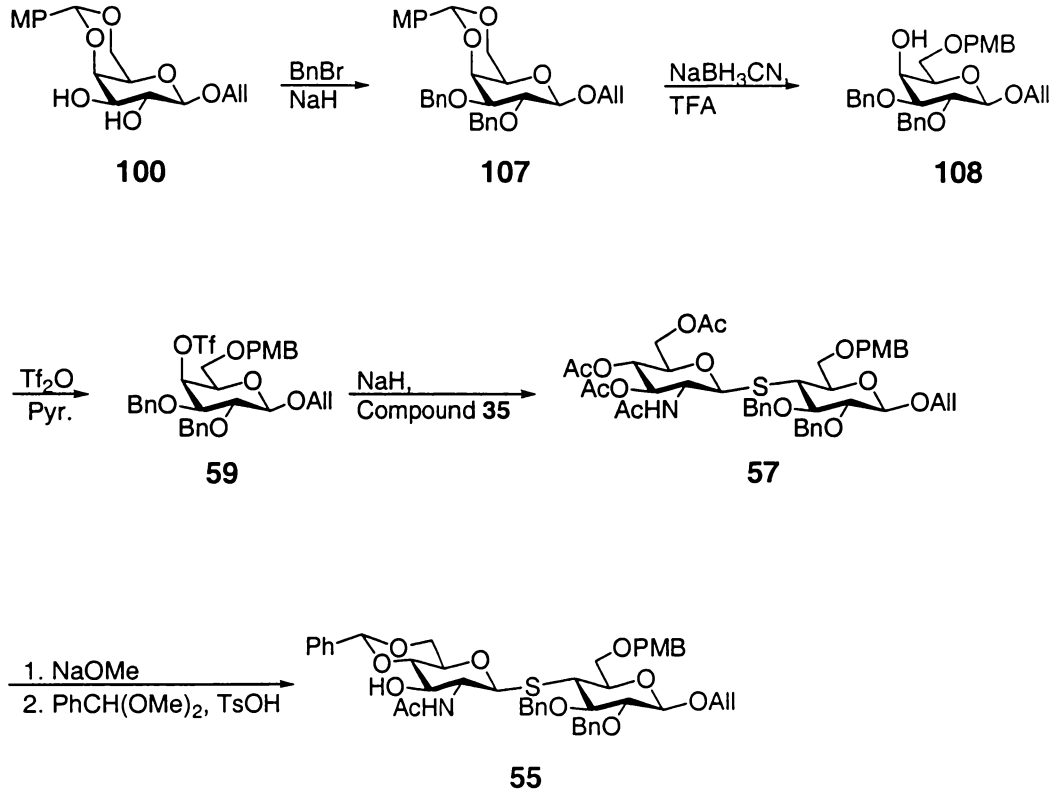
(DMF) at r. t. furnished thiol **105** in 94% yield. Exposure of thiol **105** to a relatively weaker base, potassium carbonate (K_2CO_3), in *N*,*N*-dimethylformamide (DMF) at 0 °C for 10 min, followed by addition of 2–3 equivalents of glycosyl chloride **75**, gave the same *S*-linked disaccharide in 86% yield. Only the desired β anomer was observed in this reaction, as confirmed by 1D and 2D (gCOSY, HSQC) NMR spectroscopy with a coupling constant of $J_{H1, H2}$ = 10.8 Hz (for spectra, refer to Appendix II). Conversion of **56** to **106** was achieved in 95% yield, with an α, β anomeric ratio of 1:2, via a two-step process involving isomerization of the allyl group with hydrogen (H_2) pre-activated (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate in terahydrofuran (THF), followed by cleavage of the resulting propenyl ether with iodine (I_2) and sodium bicarbonate ($NaHCO_3$) in tetrahydrofuran (THF) and water.[99] Treatment of disaccharide **106** with trichloroacetonitrile (CCl_3CN) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane (CH_2Cl_2) gave trichloroacetimidate **54** in 86% yield, with an α, β anomeric ratio of 6:1, as shown in Scheme 26.

3.2.2. Synthesis of Acceptor 55

The synthesis of acceptor **55** began with diol **100** (for synthesis of diol **100**, refer back to Scheme 23) as shown in Scheme 27. Hence, diol **100** was treated with sodium hydride (NaH) in *N*,*N*-dimethylformamide (DMF) at 0 °C for 10 min and then reacted with benzyl bromide (BnBr) to give compound **107** in 93% yield, which upon regioselective reductive cleavage with sodium cyanoborohydride ($NaBH_3CN$) and



Scheme 26. Synthesis of Trichloroacetimidate 54.

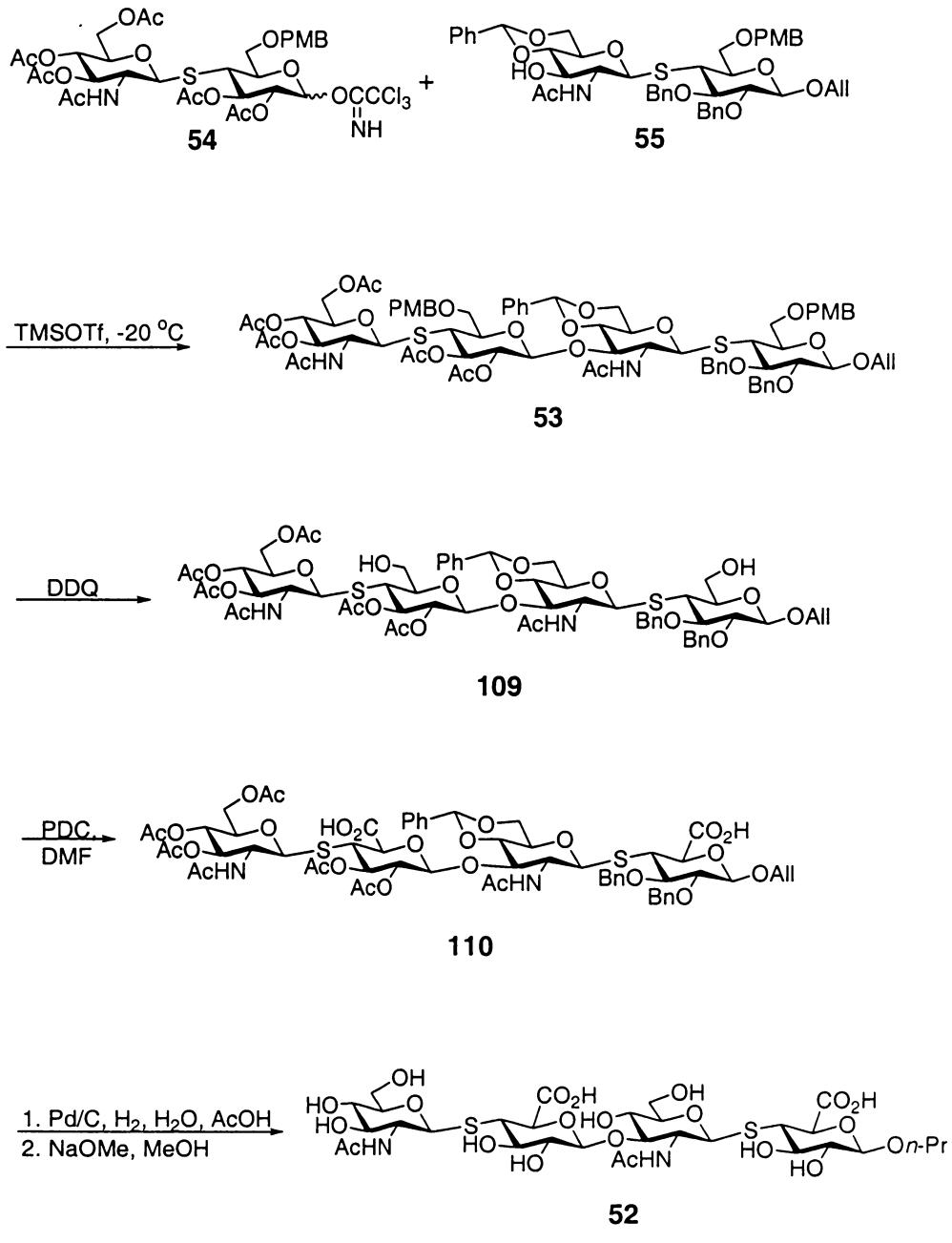


Scheme 27. Synthesis of Acceptor 55.

trifloroacetic acid (TFA) in the presence of 4 Å MS in *N*,*N*-dimethylformamide (DMF) afforded the 4-OH isomer **108** as the major product in 65% yield, along with a trace of the 6-OH isomer as a byproduct. Activation of alcohol **108** to triflate **59** was achieved in nearly quantitative yield via treatment with triflic anhydride (Tf_2O) in the presence of pyridine in dichloromethane (CH_2Cl_2), The resulting triflate **59** was exposed to pretreated thiol **35** with sodium hydride (NaH) in *N*,*N*-dimethylformamide (DMF) at 0 °C to afford the desired *S*-disaccharide **57** in 75% yield. The *S*-(1→4) linkage was confirmed to be β by 1D and 2D (gCOSY, HSQC) NMR spectroscopy, with a coupling constant of $J_{H1,\,H2}$ = 10.2 Hz (for spectra, refer to Appendix II). Deacetylation of compound **57** with sodium methoxide (NaOMe) in 1:5 dichloromethane (CH_2Cl_2) and methanol, followed by 4,6-regioselective protection of the resulting triol with benzaldehyde dimethyl acetal in the presence of a catalytic amount of *p*-toluenesulfonic acid (TsOH) in acetonitrile (CH_3CN) at r. t., rendered acceptor **55** as a precipitate in 93% yield.

3.2.3. Synthesis of *S*-/*O*-linked HA Tetrasaccharide Mimetics

As acceptor **55** is barely soluble in dichloromethane (CH_2Cl_2), reverse addition was employed in the condensation of trichloroacetimidate **54** and acceptor **55** as shown in Scheme 28. Hence, acceptor **55** was suspended in dichloromethane (CH_2Cl_2) at –15 °C under the protection of nitrogen (N_2) and treated with a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) for 20 min, and then a solution of trichloroacetimidate **54** in dichloromethane (CH_2Cl_2) was added dropwise, to give tetrasaccharide **53** in 58% yield. The (1→3)-linkage was confirmed to be β by 1D and 2D



Scheme 28. Synthesis of *S*-/*O*-linked HA Tetrasaccharide Mimetics.

(gCOSY, HSQC, TOCSY, HMBC) NMR spectroscopy with a coupling constant of $J_{H1,H2}$ = 6.6 Hz (for spectra, refer to Appendix II). Removal of the *p*-methoxybenzyl (PMB) groups with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 15:1 dichloromethane (CH_2Cl_2) and water at r. t. gave diol **109** in 60% yield. As predicted, sulfur presented problems in the following oxidation and debenzylation reactions. TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) reagent, a very efficient reagent to oxidize primary hydroxyl groups to carboxylic acids in most cases, did not afford the desired carboxylic acid here, while a combination of the Swern oxidation of primary hydroxyl groups to the aldehyde and oxidation of the resulting aldehyde to carboxylic acid with sodium chlorate ($NaClO_2$) also failed. Finally, to our amazement, we found that oxidation of diol **109** with pyridinium dichromate (PDC) in *N*,*N*-dimethylformamide (DMF) could afford us the desired tetrasaccharide **110** in 79% yield. It is well known that a benzylidene ring and benzyl groups can be unveiled with Pd/C or $Pd(OH)_2/C$ in a hydrogen (H_2) atomsphere. However, in this particular case, all attempts with different combinations of catalysts and solvents gave negative results. Finally, we found that under very strong conditions, i.e., an excess of Pd/C in 80% acetic acid under a pressure of 50 psi of hydrogen (H_2), we could push the reaction to give the desired tetrasaccharide with both benzylidene ring and benzyl groups removed in 31% yield.[100] Deacetylation of the resulting tetrasaccharide with sodium methoxide (NaOMe) in 1:5 dichloromethane (CH_2Cl_2) and methanol provided the target *S*-/*O*-linked HA tetrasaccharide mimetic **52** in nearly quantitative yield. Tetrasaccharide **52** was characterized extensively via 1D and 2D (gCOSY, HSQC, TOCSY, HMBC, etc.) NMR spectroscopy (for spectra, refer to Appendix II). Negative-

ion mode ESI mass spectroscopy as shown in Figure 10 confirms the molecular composition as shown by 848.9 $[M - H]^-$, 870.9 $[M - 2H + Na]^-$, 886.9 $[M - 2H + K]^-$.

3.3. Synthesis of Higher Order *S*-/*O*-linked HA Oligosaccharide Mimetics

Based on the success of the synthesis of *S*-/*O*-linked HA tetrasaccharide mimetics, significant advances were achieved toward the synthesis of higher order *S*-/*O*-linked HA oligosaccharide mimetics. However, although universal *S*-linked disaccharide building blocks **60** and **64** seemed to be promising, unforeseen problems forced us to revise our strategies. In particular, the introduction and presence of the sulfur functionality restrained our choice of protective groups and reagents. The ways in which steric and/or electronic effects of protective groups, as well as a longer chain, affect the stability and/or reactivity of glycosyl donors and acceptors is not predictable. However, to our gratification, the synthesis of *S*-/*O*-linked HA hexasaccharide mimetics has been accomplished via plan B as detailed below. This strategy should allow us to get rapid access to eight-mer and beyond.

3.3.1. Efforts to Higher Order *S*-/*O*-linked HA Oligosaccharide Mimetics via Plan A

In order to cut down on the number of the steps required for the synthesis of higher order *S*-/*O*-linked HA oligosaccharide mimetics, disaccharide **60** as shown in Figure 11 was first targeted as a universal building block. As we described above, the allyl group could be selectively deprotected via the two-step process involving isomerization and oxidation, and the disaccharide would also serve as a donor if activated

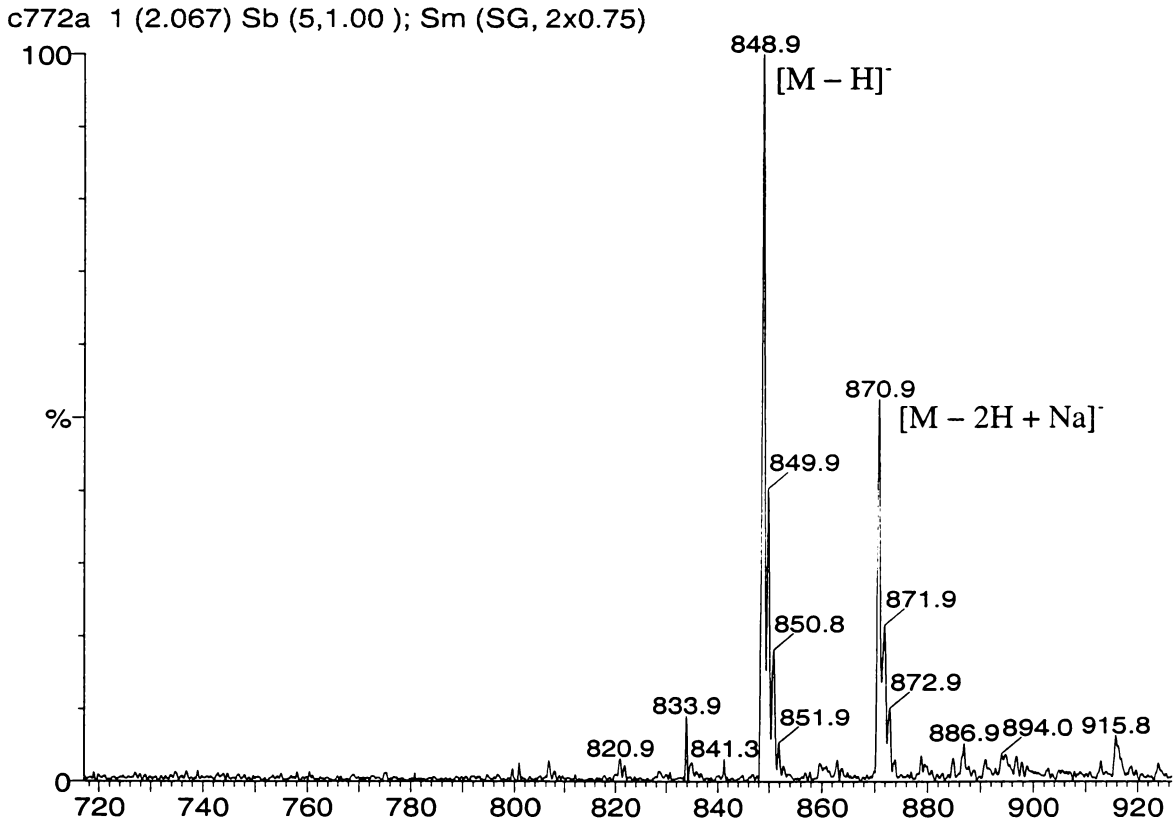
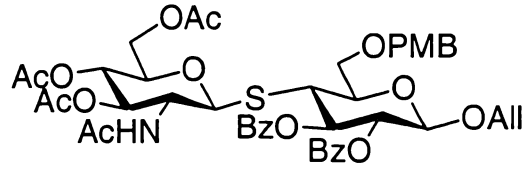


Figure 10. Negative-Ion Mode ESIMS of Tetrasaccharide 52.



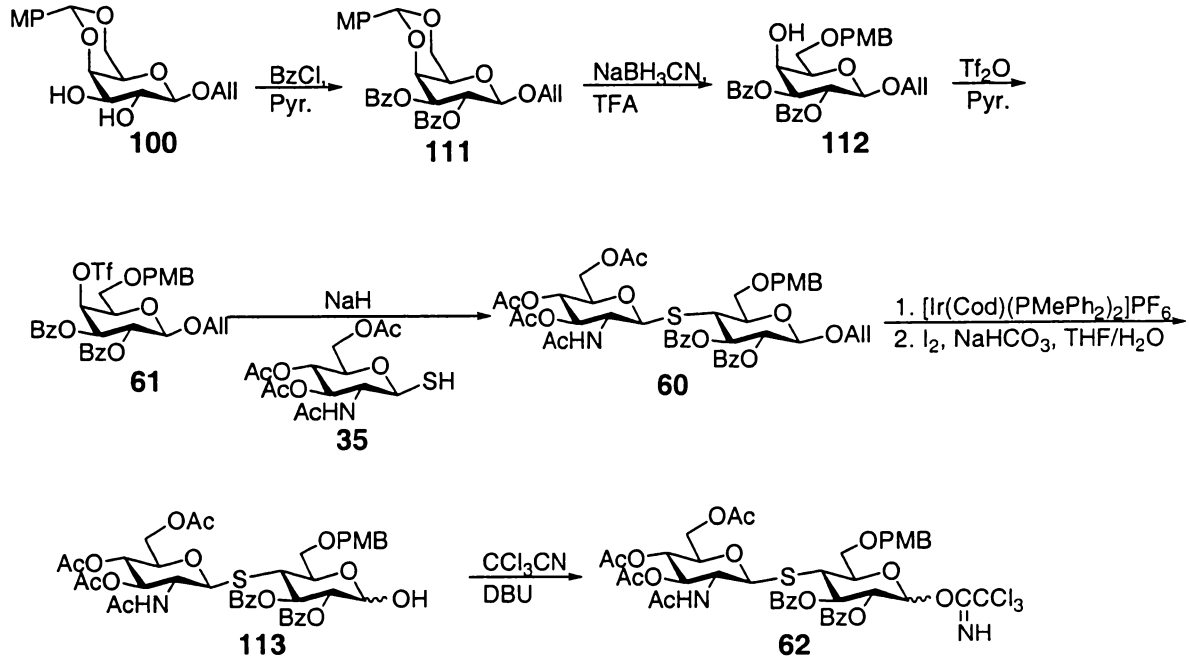
60

Figure 11. Design of Universal Disaccharide Building Block 60 (Plan A).

as the trichloroacetimidate. According to Pozsgay,[75] acetyl groups could be selectively unmasked in the presence of benzoyl groups via treatment with tetrafluoroboric acid (HBF_4). This gave us the possibility of generating acceptor **63** from disaccharide **60** by selective deacetylation and 4,6-protection.

3.3.1.1. Synthesis of Universal *S*-linked Disaccharide Building Block 60

The synthesis of triflate **61** began with diol **100** (for synthesis of diol **100**, refer back to Scheme 23) as shown in Scheme 29. Hence, diol **100** was stirred with benzoyl chloride (BzCl) in pyridine at r. t. overnight to afford compound **111** in 89% yield, which upon regioselective reductive cleavage of the benzylidene ring to a free hydroxyl group and *p*-methoxybenzyl (PMB) ether with sodium cyanoborohydride ($NaBH_3CN$) and trifluoroacetic acid (TFA) in the presence of 4 Å MS in *N*,*N*-dimethylformamide (DMF) afforded the desired 4-OH isomer **112** in 80% yield, along with a trace of the 6-OH isomer as byproduct. Treatment of alcohol **112** with triflic anhydride (Tf_2O) in the

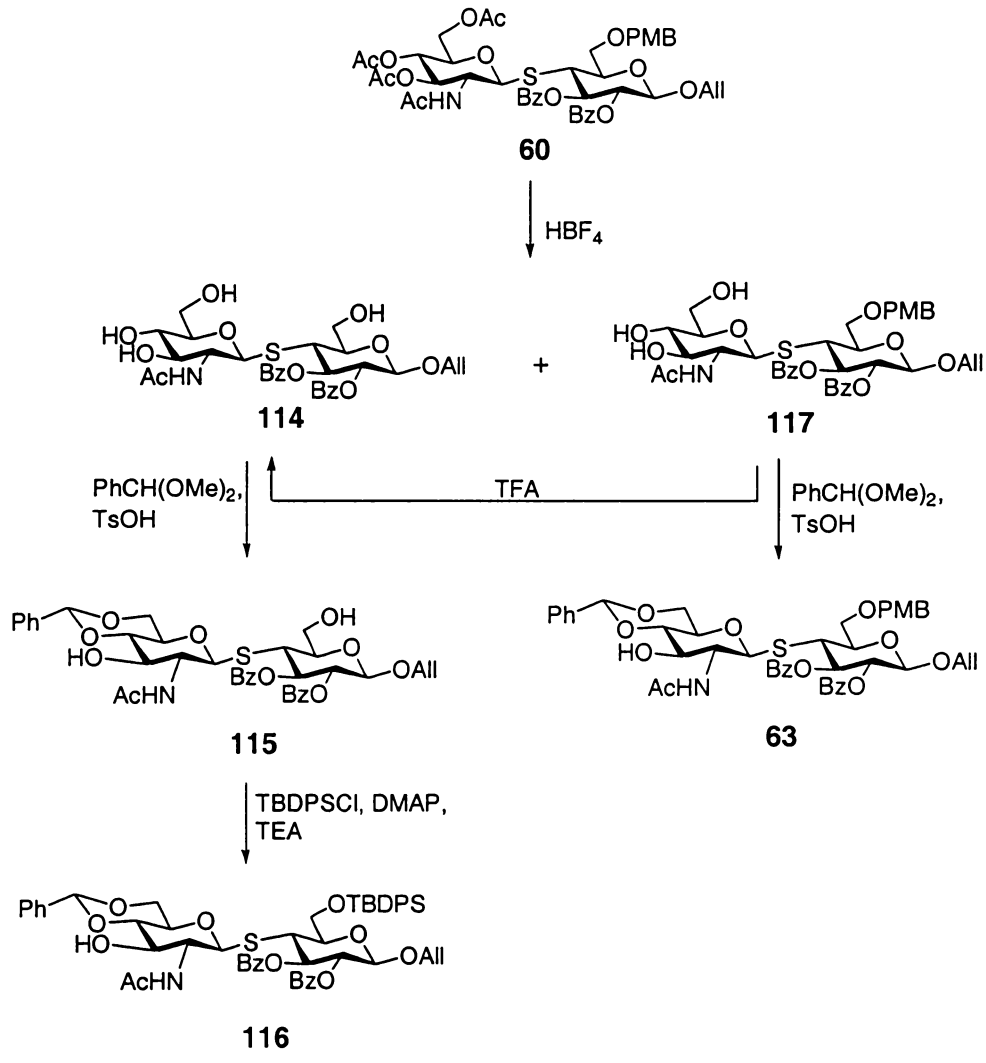


Scheme 29. Synthesis of Trichloroacetimidate 62.

presence of pyridine in dichloromethane (CH_2Cl_2) at 0 °C overnight gave triflate **61** in nearly quantitative yield. Base-mediated coupling of triflate **61** and pretreated thiol **35** (for synthesis of **35**, refer back to Scheme 24) with sodium hydride (NaH) at 0 °C afforded the desired β disaccharide **60** in 53% yield. Compound **60** was converted to **113**, with an α, β anomeric ratio of 1:2, in 95% yield via the two-step process involving isomerization of the allyl group with hydrogen (H_2) pre-activated (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate in terahydrofuran (THF) for 3 days, followed by cleavage of the resulting propenyl ether with iodine (I_2) and sodium bicarbonate ($NaHCO_3$) in tetrahydrofuran (THF) and water at 0 °C. Unlike that of compound **54**, isomerization of compound **60** required reflux, due probably to the deactivating effect of benzoyl group at C-2. Treatment of disaccharide **113** with trichloroacetonitrile (CCl_3CN) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane (CH_2Cl_2) at r. t. for 1 h gave the desired trichloroacetimidate **62**, with an α, β anomeric ratio of 6:1, in 86% yield.

3.3.1.2. Attempted Synthesis of *S*-/*O*-linked HA Tetrasaccharide Mimetic 118

Although trichloroacetimidate **62** was successfully synthesized, a problem arose in the synthesis of acceptor **63**. Instead of the desired compound **117**, deacetylation of disaccharide **60** with tetrafluoroboric acid (HBF_4) in 1:5 dichloromethane (CH_2Cl_2) and methanol gave predominantly compound **114** (71%), with only a small amount of the desired compound **117** (13%). However, an alternative acceptor **116** was obtained by following the procedure as shown in Scheme 30. Hence, conversion of compound **117** to

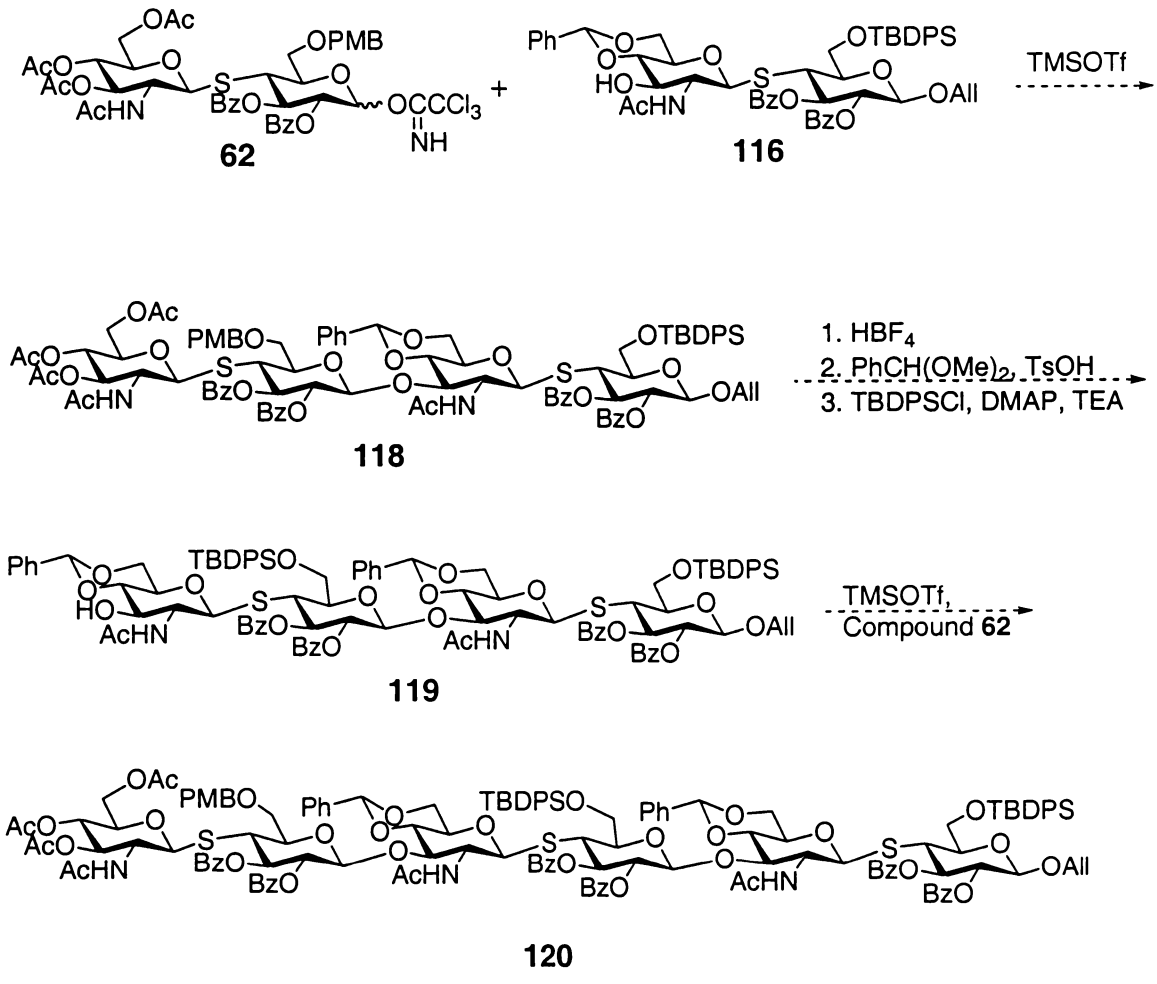


Scheme 30. Synthesis of Acceptors 63 and 116.

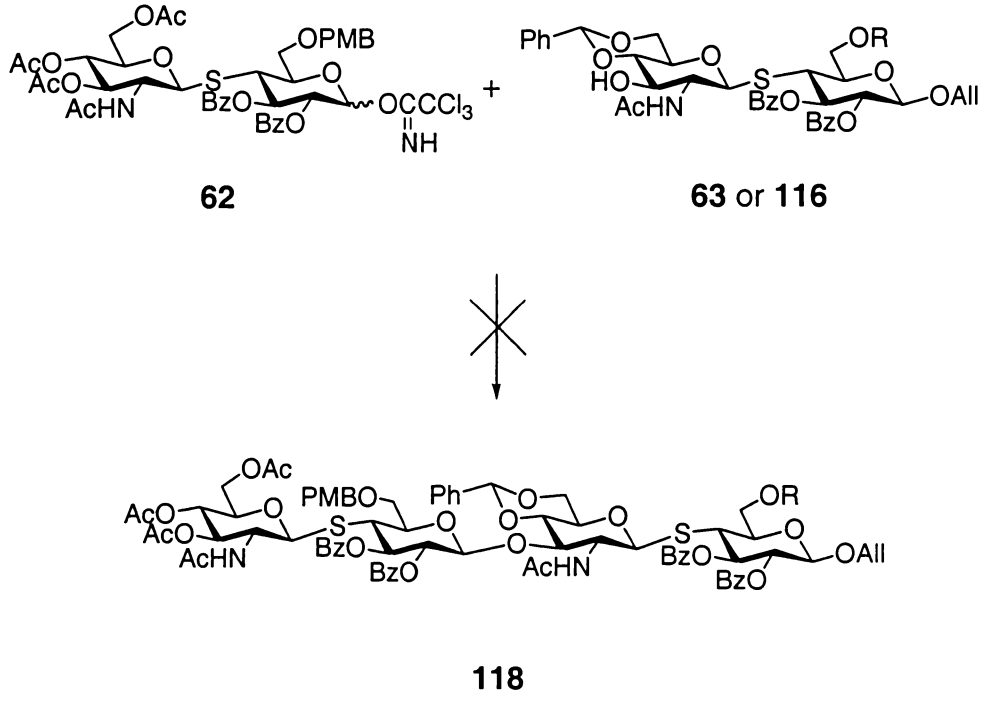
compound **114** was achieved via treatment with trifluoroacetic acid (TFA) in dichloromethane (CH_2Cl_2).[101] Disaccharide **114** was treated with benzaldehyde dimethyl acetal in the presence of a catalytic amount of *p*-toluenesulfonic acid (TsOH) in dry acetonitrile to afford compound **115** as a precipitate in 72% yield. Selective protection of the primary alcohol with the *tert*-butyldiphenylsilyl (TBDPS) group via treatment with *tert*-butyldiphenylsilyl chloride (TBDPSCl) and triethylamine (TEA) in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP) in dichloromethane (CH_2Cl_2) gave an alternative acceptor **116** in 91% yield.[102,103] Although this unexpected problem caused a slight change in our strategy, the following revised plan A as shown in Scheme 31 still seemed to be promising. Unfortunately, all attempts (different combinations of catalysts, solvents, and reaction temperatures) to condense trichloroacetimidate **62** with either acceptor **116** or acceptor **63** (obtained via treatment of **117** with benzaldehyde dimethyl acetal and *p*-toluenesulfonic acid (TsOH) in acetonitrile.) together failed, due no doubt to the deactivating effect of the C-2 benzoyl group of the trichloroacetimidate (as shown in Scheme 32). This strategy was thus discarded.

3.3.2. Efforts to Higher Order *S*-/*O*-linked HA Oligosaccharide Mimetics via Plan B

As a replacement of disaccharide **60**, an alternative universal disaccharide building block **64** was projected as shown in Figure 12. The protective groups were strategically set up so that the levulinoyl group could be selectively deprotected in the presence of acetyl groups, and the resulting disaccharide would serve as a glycosyl acceptor (3′-OH free); the disaccharide could also serve as a C-1 glycosyl donor after 1-

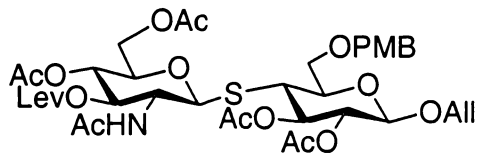


Scheme 31. Revised Plan A.



R = PMB or TBDPS

Scheme 32. Efforts to *S*-/*O*-linked HA Tetrasaccharide via Plan A.



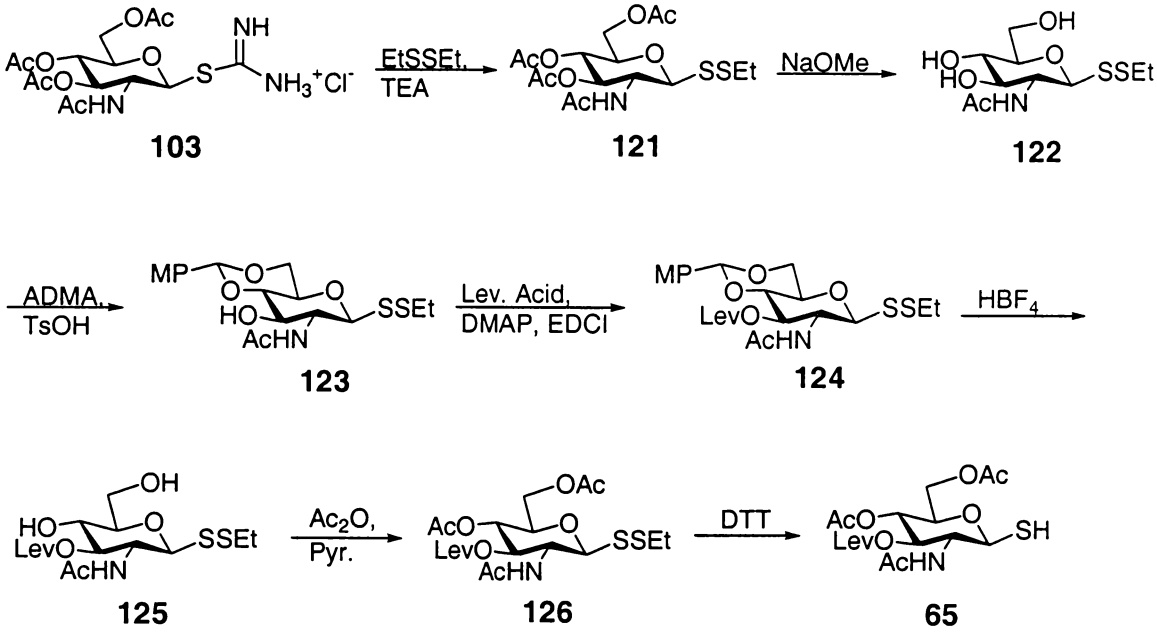
64

Figure 12. Design of Universal Disaccharide Building Block 64 (Plan B).

deallylation and activation as trichloroacetimidate. In addition, all the protective groups could be unveiled with lithium hydroxide (LiOH) or sodium methoxide (NaOMe) in the final deprotection.

3.3.2.1. Synthesis of *S*-linked Disaccharide Donor 66 and Acceptor 67

The synthesis of thiol **65** proceeded with peudothiourea **103** (for synthesis of peudothiourea **103**, refer back to Scheme 24) as shown in Scheme 33. Hence, treatment of peudothiourea **103** with ethyl disulfide in the presence of triethylamine (TEA) in methanol gave disulfide **121** in 68% yield.[104, 105] In order to manipulate the protective groups, compound **121** was first treated with sodium methoxide (NaOMe) in 1:5 dichloromethane (CH_2Cl_2) and methanol (MeOH) to unmask the acetyl groups. The resulting triol **122** was then stirred with anisaldehyde dimethyl acetal (ADMA) in the presence of a catalytic amount of *p*-toluenesulfonic acid (TsOH) in acetonitrile at r. t. for about 2 h, and acetal exchange occurred, resulting in the formation of a precipitate of



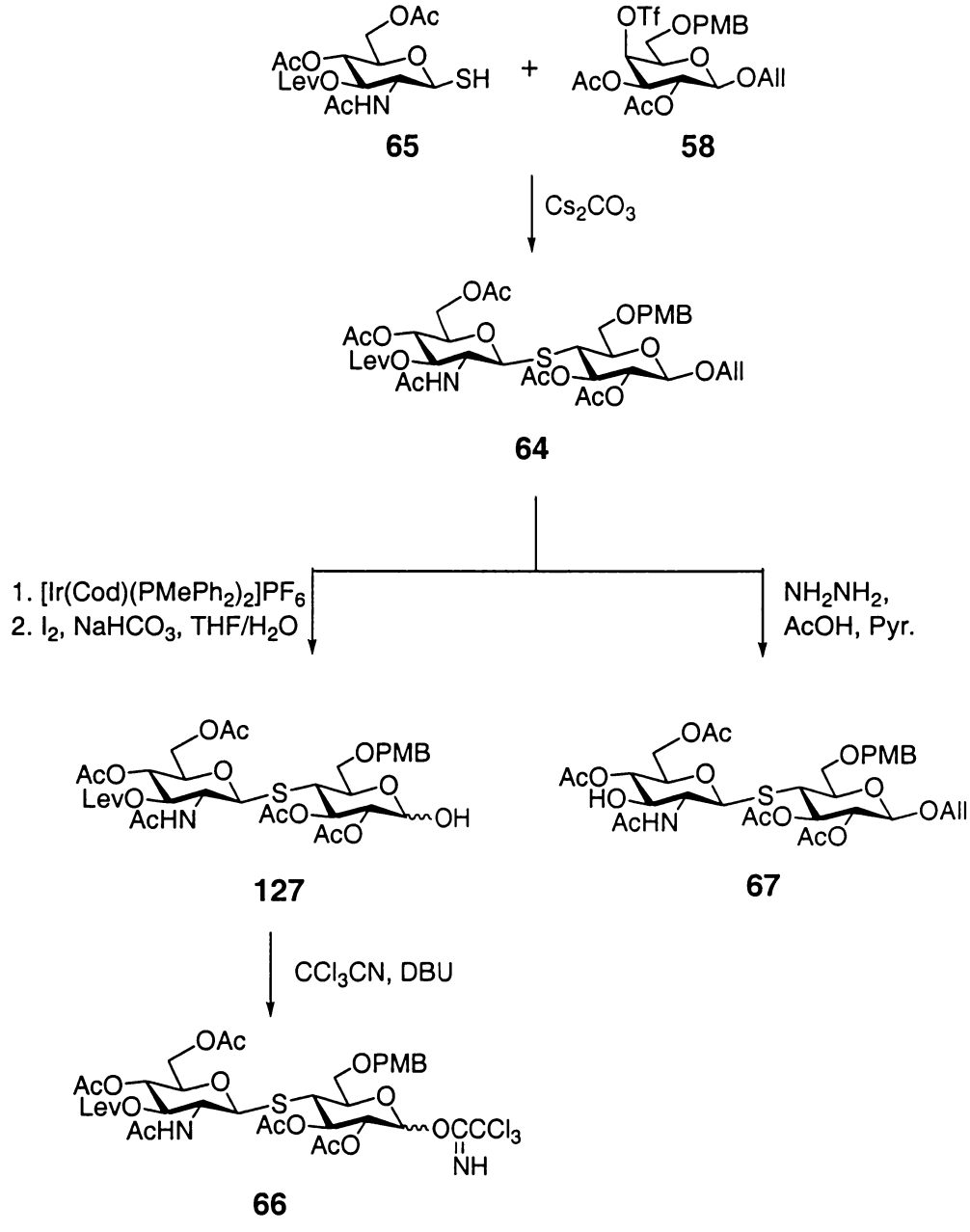
Scheme 33. Synthesis of Thiol 65.

123 in 86% yield. Treatment of compound with levulinic acid and 1-(3-dimethylaminopropyl)-3-ethylcarbdiimide hydrochloride (EDCI) in the presence of a catalytic amount of 4-dimethyaminopyridine (DMAP) in dichloromethane (CH_2Cl_2) afforded compound **124** in 80% yield. In order to make the final deprotection easier, the benzylidine ring was replaced with acetyl groups as follows. Compound **124** was treated with tetrafluoroboric acid in methanol at r. t. for 1 h to give diol **125**, and then the resulting diol **125** was acetylated with acetic anhydride in the presence of pyridine to afford compound **126** in 84% yield. Treatment of disulfide **126** with dithiothreitol (DTT) in the presence of triethylamine (TEA) in tetrahydrofuran (THF) and methanol (MeOH) afforded the desired thiol **65** in 80% yield.[104] Base-promoted S_N2 coupling of thiol **65** and triflate **58** was achieved via treatment with cesium carbonate (Cs_2CO_3) in *N,N*-dimethylformamide (DMF) at 0 °C for 2 h to provide the desired disaccharide **64** in 88% yield. Only the β isomer was observed in this reaction, as confirmed by 1D and 2D NMR spectroscopy with a coupling constant of $J_{H1, H2}$ = 10.8 Hz (for spectra, refer to Appendix II). Deallylation of disaccharide **64** by following the two-step process involving isomerization of the allyl group with hydrogen (H_2) pre-activated (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate in terahydrofuran (THF) for 3 days, followed by cleavage of the resulting propenyl ether with iodine (I_2) and sodium bicarbonate ($NaHCO_3$) in tetrahydrofuran (THF) and water at 0 °C afforded disaccharide **127**, with an α, β anomeric ratio of 1:2, in 92% yield. Treatment of disaccharide **127** with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane (CH_2Cl_2) at r. t. for 1 h

rendered the desired trichloroacetimidate **66**, with an α, β anomeric ratio of 8:1, in 82% yield. Treatment of disaccharide **64** with hydrazine in the presence of acetic acid (AcOH) in pyridine furnished acceptor **67** in 89% yield (as shown in Scheme 34).

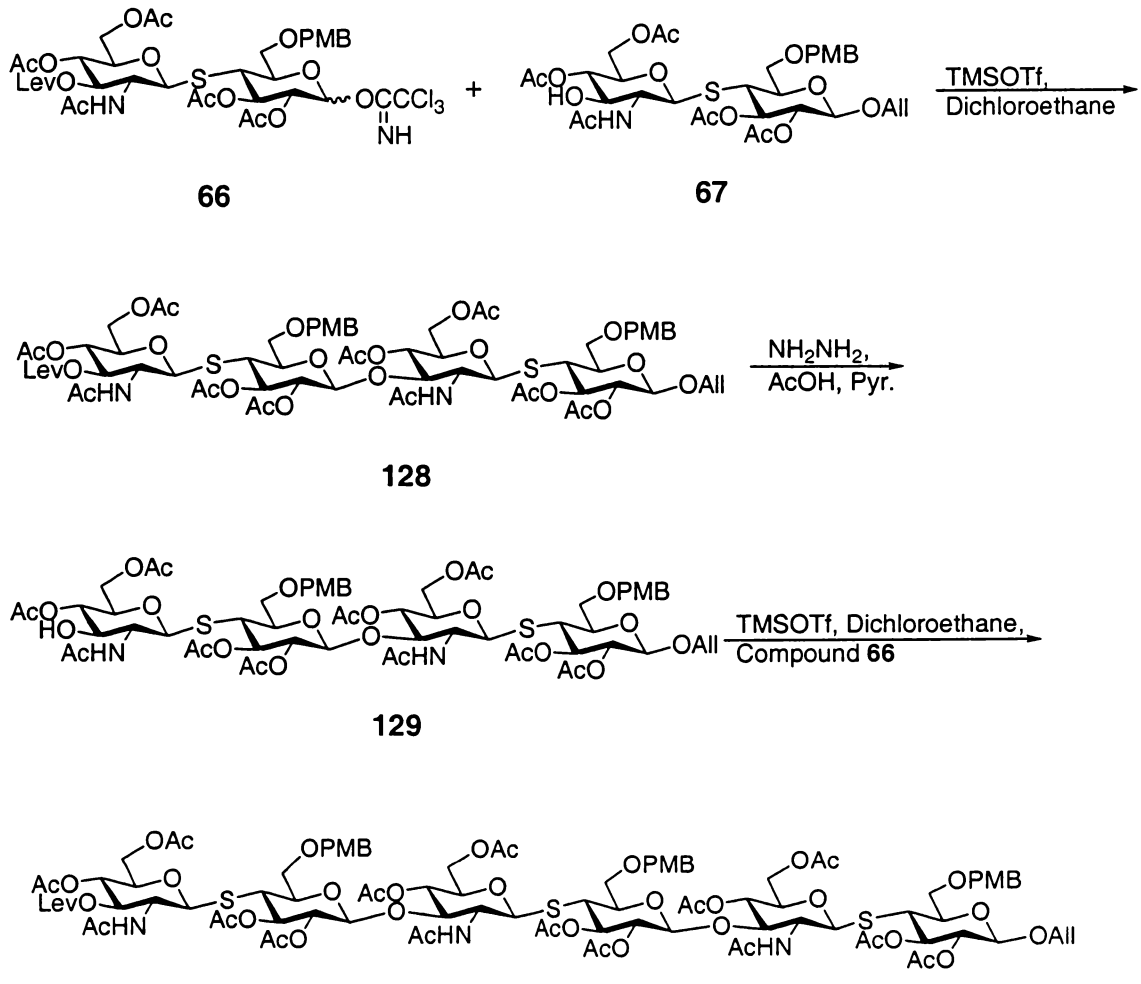
3.3.2.2. Synthesis of Higher Order *S*-/*O*-linked HA Oligosaccharide Mimetics

Condensation of trichloroacetimidate **66** with acceptor **67** in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in dichloromethane (CH_2Cl_2) at –15 °C gave the desired tetrasaccharide **128** in very poor yield (<20%). However, we found that by simply changing the solvent from dichloromethane (CH_2Cl_2) to 1,2-dichloroethane ($ClCH_2CH_2Cl$), the yield of tetrasaccharide **128** could be improved up to 69%. The (1→3)-linkage of tetrasaccharide **128** was comfirmed to be β by 1D and 2D (gCOSY, HSQC, TOCSY, HMBC, etc) NMR spectroscopy, with a coupling constant of $J_{H1, H2}$ = 7.8 Hz (for spectra, refer to Appendix II). Deprotection of tetrasaccharide **128** with hydrazine in the presence of acetic acid in pyridine provided tetrasaccharide acceptor **129** in 88% yield. However, when acceptor **129** was resubjected to trichloroacetimidate **66** and a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in 1,2-dichloroethane at –15 °C, only a small amount of hexasaccharide **130** was obtained (<10%), due probably to the deactivating effect of the prolonged acceptor chain. To our amazement, however, we found that the yield of hexasaccharide **130** could be improved to 46% by employing a reverse addition strategy as follows. Hence, acceptor **129** was dissolved in 1,2-dichloroethane and treated

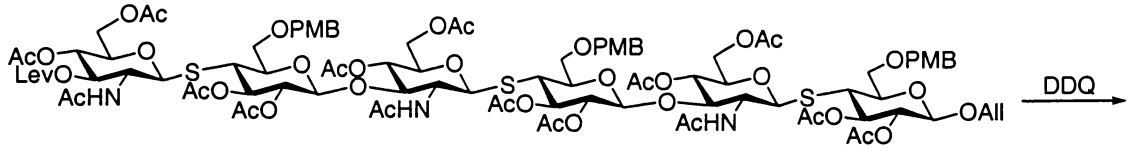


Scheme 34. Synthesis of Glycosyl Donor 66 and Acceptor 67.

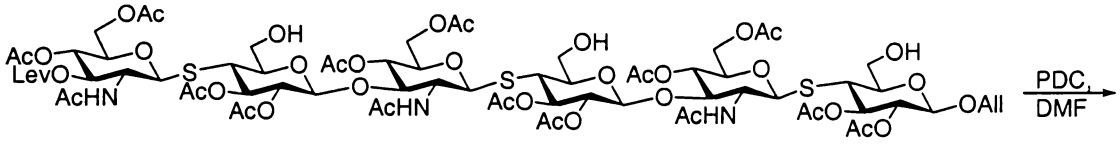
with a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) at –15 °C for about 10 min, followed by addition of 1.5 equivalents of trichloroacetimidate **66**. After 1 h, another 1.5 equivalents of trichloroacetimidate **66** were added, followed by addition of another catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (as shown Scheme 35). The newly formed (1→3)-linkage of hexasaccharide **130** was comfirmed to be also β by 1D and 2D (gCOSY, HSQC, HMBC, TOSCY, etc) NMR spectroscopy, with a coupling constant of $J_{H1, H2}$ = 8.4 Hz (for spectra, refer to Appendix II). Treatment of hexasaccharide **130** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 15:1 dichloromethane (CH_2Cl_2) and water at r. t. for 2 h gave hexasacchraride **131** in 83% yield. Oxidation of hexasaccharide **131** to carboxylic acid **132** was achieved in 69% yield via treatment with pyridinium dichromate (PDC) in *N*,*N*-dimethylformamide (DMF) at r. t. for 3 days. Finally, deprotection of carboxylic acid **132** with lithium hydroxide (LiOH) in 1:2 tetrahydrofuran (THF) and water gave the desired *S*-/*O*-linked HA hexasaccharide mimetic **133** in 80% yield (as shown in Scheme 36). Hexasaccharide **133** was characterized extensively via 1D and 2D (gCOSY, HSQC, TOCSY, HMBC, etc.) NMR spectroscopy (for spectra, refer to Appendix II). Negative-ion mode MALDIMS as shown in Figure 13 confirms the molecular composition as shown by 1242.3100 $[M - H]^-$, 1264.2767 $[M - 2H + Na]^-$, 1280.2525 $[M - 2H + K]^-$, 1286.2227 $[M - 3H + 2Na]^-$, 1297.2186 $[M - 3H + NH_4 + K]^-$.



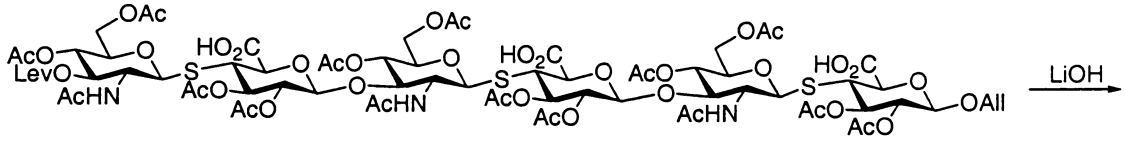
Scheme 35. Synthesis of *S*-/*O*-linked HA Hexasaccharide Mimetics.



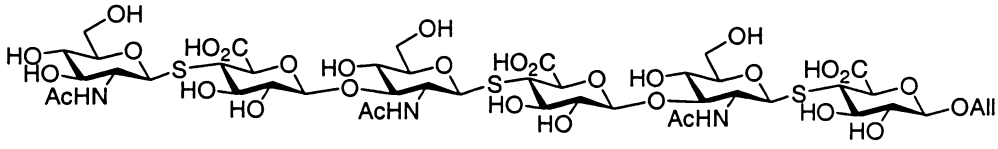
130



131



132



133

Scheme 36. Synthesis of *S*-/*O*-linked HA Hexasaccharide Mimetics (cont'd).

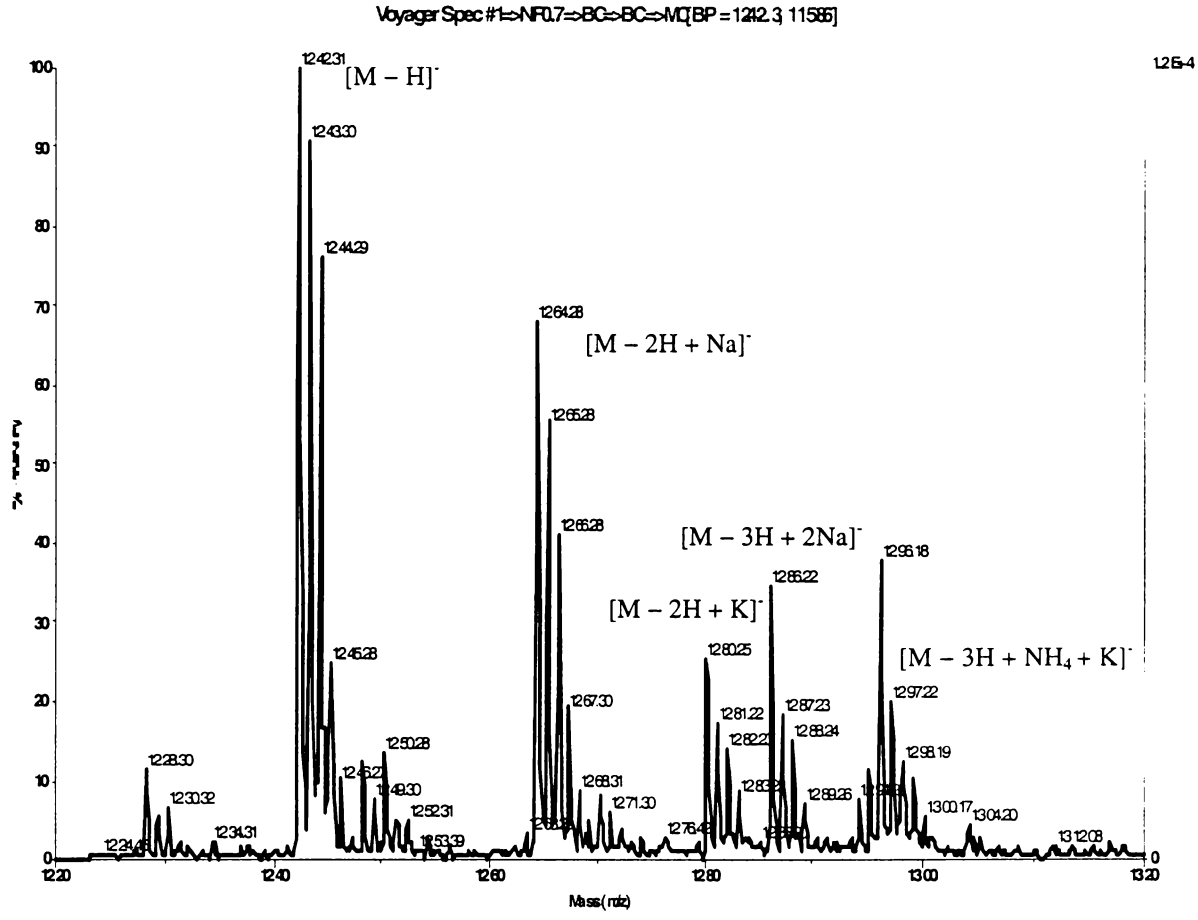


Figure 13. Negative-Ion Model MALDIMS Spectrum of Hexasaccharide 133.

IV. CONCLUSIONS

With respect to the objectives set forth in section 2.1, a *C*-linked disaccharide acceptor was successfully synthesized via SmI_2-promoted coupling reaction of a properly protected sulfone and a properly protected aldehyde. The synthesis of *C*-/*O*-linked HA tetrasaccharide mimetics has been accomplished by my co-worker, Dr. Zhong-Xu Ren, by using this disaccharide as a building block. As for objective No. 2, the synthesis of *S*-/*O*-linked HA tetrasaccharide mimetics was accomplished. Target compounds were obtained through trichloroacetimidate glycosylation of two strategically protected *S*-disaccharides as building blocks, both of which were obtained via base-mediated coupling of a thiol donor and two properly protected triflates, respectively.

Based on the chemistry developed in the synthesis of *S*-/*O*-linked HA tetrasaccharide mimetics, the synthesis of *S*-/*O*-linked hexasaccharide mimetics was accomplished via trichloroacetimidate glycosylation from a universal *S*-linked disaccharide unit that is strategically protected to be used as either a C-1 glycosyl donor (activated as trichloroacetimidate) or as a glycosyl acceptor (3'-OH free). This strategy should allow us to get rapid access to eight-mer and beyond.

All the *C*-/*O*-linked and *S*-/*O*-linked HA oligosaccharide mimetics prepared herein will provide useful information for the synthesis and characterization of higher order HA oligosaccharide mimetics and related compounds. The "block strategy' employed here, i.e., of linking of *S*- or *C*-linked disaccharides by normal *O*-linkages, is a novel and practical approach to such oligosaccharide analogs. To date, nothing has been

documented in the literature using the idea of blockwise "mixed" oligosaccharide synthesis. These compounds might also find use as probes in the NMR spectral and molecular studies, as well as to serve as hyaluronidase inhibitors. In addition, their potential as antimetastatic agents will be evaluated.

V. EXPERIMENTAL SECTION

General methods.—^{1}H (250 MHz, 300 MHz, and 600 MHz) and ^{13}C (62.5 MHz, 75 MHz, and 150 MHz) NMR spectra were recorded at 25 °C with a Bruker AC 250, a Varian Mecury 300, or a Varian Inova 600 instrument, respectively. Chemical shifts are given in ppm relative to an internal standard of tetramethylsilane (TMS) for ^{1}H, and relative to the signal for $CDCl_3$ (δ 77.0) or DMSO-d_6 (δ 39.5) for ^{13}C, unless otherwise stated. Apparent, first-order multiplicities are indicated by s, singlet; d, doublet; dd, doublet of doublets; t, triplet; dt, doublet of triplets; q, quartet, and m, multiplet. All assignments of disaccharides, tetrasaccharides and hexasaccharides were confirmed with the aid of two-dimensional experiments (gCOSY, HSQC, HMBC and TOCSY), which were recorded with a Varian Inova 600. Column chromatography was performed on 60 Å (63–200 μm, termed "coarse") silica gel (Sorbent Technologies) and fractions were monitored by TLC on Silica Gel 60 F_{254} (0.2-mm aluminum-backed plates, E. Merck) by detection with 254 nm UV light and then spray–heat development using a *p*-anisaldehyde–sulfuric acid reagent. Melting points were measured with a Thomas–Hoover Capillary melting point apparatus. Optical rotations were performed with a Perkin–Elmer 241 polarimeter (1-dm cell) at 20 °C. ESI mass spectra analyses were obtained on a Micromass VG Quattro II electrospray instrument. MALDI mass spectra analyses were obtained on a Voyager-DE PRO BioSpectrometry Workstation. Elemental analyses were furnished by Atlantic Microlab, Inc. of Atlanta, GA. All solvents were dried and distilled by standard methods

unless otherwise stated. The (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate catalyst was purchased from Aldrich Chemical Co.

***p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (68)**. To a solution of compound **23** (18.34 g, 47.2 mmol) and *p*-methoxylphenol (8.80 g, 70.97 mmol, 1.5 equiv) in dry CH_2Cl_2 (250 mL) was TMSOTf (2 mL) added at 0 °C. The reaction was stirred at 0 °C for 2 h, and then it was quenched with tirethylamine (TEA). The mixture was washed with aq $NaHCO_3$ and water, respectively and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (4:1 to 3:1 hexanes–EtOAc) to give compound **68** as a white amorphous solid (18.94 g, 41.90 mmol, 89%). The data match those reported in the literature.[77]

***p*-Methoxyphenyl β-D-galactopyranoside (69)**. To a solution of compound **68** (20.5 g, 45.4 mmol) in dry CH_2Cl_2 (50 mL) and dry MeOH (250 mL) was added NaOMe (25% in MeOH, 0.25 mL). The reaction was stirred at r. t. for 1 h, after which time the reaction was quenched with Dowex 50 × 2-100 (H^+ form). The suspension was filtered and evaporated to afford tetraol **69** as a white amorphous solid (12.69 g, 44.0 mmol, 97%), which was used in the next step without characterization. TLC (9:1 CH_2Cl_2–MeOH): R_f 0.1; mp 158–160 °C; $[\alpha]_D$ –35.7° (*c* 1.1, H_2O).

***p*-Methoxyphenyl 4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (70)**. To a suspension of tetraol **69** (11.00 g, 38.5 mmol) in dry CH_3CN (250 mL) were added anisaldehyde dimethyl acetal (ADMA, 69.0 mL, 0.40 mol) and *p*-toluenesulfonic acid (0.75 g, 3.9 mmol, 0.1 equiv). The solution was stirred at r. t. for about 4 h, after this time the reaction was quenched with triethylamine (TEA). The suspension was filtered and the solid was washed with EtOAc and MeOH sequentially to afford compound **70** as a white amorphous solid (13.07 g, 32.2 mmol, 84%). TLC (9:1 CH_2Cl_2–MeOH): R_f 0.5; mp 224–226 °C; $[\alpha]_D$ –74.9° (*c* 1.0, DMSO); ^{1}H NMR (250 MHz, DMSO-d_6): δ 7.37 (d, 2 H, ArH), 7.01 (d, 2 H, ArH), 6.91 (d, 2 H, ArH), 6.86 (d, 2 H, ArH), 5.51 (s, 1 H, CH_3OPhCH), 5.26 (d, 1 H, H-2), 5.02 (d, 1 H, H-3), 4.83 (d, 1 H, H-1, $J_{H1, H2}$ = 6.5 Hz), 4.10 (s, 1 H, H-4), 4.02 (s, 2 H, H-6), 3.74 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.67 (s, 1 H, H-5), 3.58 (m, 1 H, OH); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 159.4, 154.3, 151.3, 131.0, 127.5, 117.6, 114.4, 113.2, 101.5, 99.7, 75.8, 71.7, 69.7, 68.4, 66.0, 55.3, 55.1; ESIMS (positive-ion mode): *m/z* 404.7 $[M + H^+]$, 426.7 $[M + Na]^+$, 442.6 $[M + K]^+$. Anal. Calcd for $C_{21}H_{24}O_8$ (404.72): C, 62.37; H, 5.98. Found: C, 62.30; H, 5.99. The data match those reported in Kenneth Price's dissertation.[66]

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (71)**. To a solution of diol **70** (7.35 g, 18.1 mmol) in dry DMF (40 mL) was added NaH (60% in mineral oil, 2.17 g, 54.3 mmol) at 0 °C. The reaction was stirred at 0 °C for 10 min, and then BnBr (8.49 mL, 72.4 mmol) was added dropwise. The reaction was allowed to stir and warm to r. t. over 10 h, after which time it was quenched

with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then concentrated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 to 2:1 hexanes–EtOAc) to give compound **71** as a white amorphous solid (10.0 g, 17.1 mmol, 95%). TLC (1:1 hexanes–EtOAc): R_f 0.5; mp 167–169 °C; $[\alpha]_D$ –6.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.49 (d, 2 H, ArH), 7.40–7.25 (m, 10 H, ArH), 7.06 (d, 2 H, ArH), 6.90 (d, 2 H, ArH), 6.80 (d, 2 H, ArH), 5.47 (s, 1 H, CH_3OPhCH), 5.00 (d, 1 H, H-1, $J_{H1, H2}$ = 10.7 Hz), 4.86 (m, 2 H, H-2, H-3), 4.78 (s, 2 H, $ArCH_2O$), 4.31 (d, 1 H, $ArCH_2O$), 4.15–3.99 (m, 3 H, H-6, H-4, $ArCH_2O$), 3.81 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.61 (dd, 1 H, H-5), 3.39 (s, 1 H, H-6); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 160.0, 155.2, 151.6, 138.6, 138.3, 130.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 118.9, 114.4, 113.4, 103.1, 101.2, 79.1, 78.1, 75.4, 73.6, 71.9, 69.0, 66.4, 55.6, 55.2; ESIMS (positive-ion mode): *m/z* 585.2 $[M + H]^+$, 607.2 $[M + Na]^+$, 623.2 $[M + K]^+$. Anal. Calcd for $C_{35}H_{36}O_8$ (584.67): C, 71.90; H, 6.21. Found: C, 71.84; H, 6.30. The data match those reported in Kenneth Price's dissertation.[66]

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (72).** A suspension of compound **71** (0.90 g, 1.54 mmol), $NaBH_3CN$ (0.39 g, 6.16 mmol) and 4 Å MS (0.41 g) in dry DMF (20 mL) was stirred at 0 °C for 15 min, and then a solution of trifluoroacetic acid (TFA) (0.95 mL, 12.3 mmol) in dry DMF (3 mL) was added dropwise. The reaction was allowed to stir and warm to r. t. over 10 h, after which time the mixture was filtered through a Celite bed, washed with satd $NaHCO_3$, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then concentrated to dryness. The

residue was submitted to coarse silica gel column chromatography (4:1 to 3.5:1 hexanes–EtOAc) to give compound **72** as colorless crystals (0.67 g, 1.14 mmol, 74%). TLC (2:1 hexanes–EtOAc): R_f 0.5; mp 93–95 °C; $[\alpha]_D$ –6.2° (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 7.38–7.22 (m, 12 H, ArH), 7.03 (d, 2 H, ArH), 6.85 (d, 2 H, ArH), 6.80 (d, 2 H, ArH), 5.01 (d, 1 H, $ArCH_2O$), 4.84 (d, 1 H, H-1, $J_{H1, H2}$ = 7.5 Hz), 4.81 (d, 1 H, $ArCH_2O$), 4.74 (s, 2 H, $ArCH_2O$), 4.50 (s, 2 H, $ArCH_2O$), 4.05 (d, 1 H, H-6), 3.91 (t, 1 H, H-4), 3.80 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.63 (t, 1 H, H-3), 3.56 (dd, 1 H, H-5), 2.56 (s, 1 H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 159.3, 155.2, 151.5, 138.4, 137.8, 130.1, 129.4, 128.5, 128.3, 128.1, 127.9, 127.8, 127.7, 118.6, 114.5, 113.8, 102.9, 80.6, 78.7, 75.3, 73.5, 73.4, 72.5, 68.9, 66.8, 55.6, 55.2; ESIMS (positive-ion mode): *m/z* 609.3 $[M + Na]^+$, 625.2 $[M + K]^+$. Anal. Calcd for $C_{35}H_{38}O_8$ (586.69): C, 71.65; H, 6.53. Found: C, 71.54; H, 6.60. The data match those reported in Kenneth Price's dissertation.[66]

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-*O*-trifluoromethanesulfonyl-β-D-galactopyranoside (73).** To a solution of compound **72** (10.0 g, 17.06 mmol) in dry CH_2Cl_2 (80 mL) and pyridine (3.5 mL, 43.3 mmol) was added triflic anhydride (3.5 mL, 21.3 mmol) dropwise at 0 °C. The reaction was stirred at 0 °C for 10 h, after which time it was concentrated and passed through a short plug of coarse silica gel (3:1 hexanes–EtOAc) to give triflate **73** as an unstable, pale-yellow syrup that was used in the nest step without characterization. TLC (2:1 hexanes–EtOAc): R_f 0.72.

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-4-*C*-cyano-4-deoxy-6-*O*-*p*-methoxybenzyl-β-D-glucopyranoside (74).** To a solution of triflate **73** (12.26 g, 17.06 mmol) in dry THF (40 mL) was added tetrabutylammonium cyanide (50 mL, 0.44 M in THF, 1.2 equiv) dropwise at –45 °C. The solution was allowed to stir and warm to r. t. over 4 h, at which time TLC (3:1 hexanes–EtOAc) showed complete consumption of starting material and formation of two main spots. The reaction was concentrated to dryness, and the residue was subjected to coarse silica gel column chromatography (7:1 to 5.5:1 hexanes–EtOAc) to afford compound **74** as a yellow syrup (6.40 g, 10.75 mmol, 63%). TLC (3:1 hexanes–EtOAc): R_f 0.4; $[\alpha]_D$ –19.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.34–7.20 (m, 12 H, ArH), 6.99 (d, 2 H, ArH), 6.83 (d, 2 H, ArH), 6.79 (d, 2 H, ArH), 5.01 (d, 1 H, $ArCH_2O$), 4.87 (s, 2 H, $ArCH_2O$), 4.85 (d, 1 H, H-1, $J_{H1, H2}$ = 7.5 Hz), 4.78 (d, 1 H, $ArCH_2O$), 4.47 (dd, 2 H, $ArCH_2O$), 3.71 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.78–3.64 (m, 4 H, H-2, H-5, H-6), 3.55 (t, 1 H, H-3), 2.98 (t, 1 H, H-4); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.4, 154.6, 150.2, 136.9, 136.4, 128.7, 128.4, 127.5, 127.4, 127.2, 127.1, 127.0, 117.6, 116.6, 113.7, 112.9, 101.9, 80.5, 78.4, 74.9, 74.2, 72.5, 71.4, 68.2, 54.6, 54.3, 35.0; ESIMS (positive-ion mode): *m/z* 618.2 $[M + Na]^+$, 634.2 $[M + K]^+$. Anal. Calcd for $C_{36}H_{37}NO_7$ (595.70): C, 72.59; H, 6.26; N, 2.35. Found: C, 72.59; H, 6.45; N, 2.24. The data match those reported in Kenneth Price's dissertation.[66]

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-4-deoxy-4-*C*-formyl-6-*O*-*p*-methoxybenzyl-β-D-glucopyranoside (21).** To a solution of compound **74** (1.06 g, 1.78 mmol) in dry THF (25 mL) was added DIBAl–H (7.11 mL, 1.5 M in toluene, 6 equiv) at -78 °C. The

reaction was allowed to stir and warm to r. t. over 10 h, after which time it was quenched with EtOAc, and the solution was stirred with 1.0 N H_3PO_4 (10 mL) for another 30 min at 0 °C. The mixture was then neutralized with satd $NaHCO_3$, filtered though a Celite bed, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then concentrated to dryness. The residue was submitted to a short plug of coarse silica gel (3.5:1 hexanes–EtOAc) to give compound **21** as a pale-yellow syrup (0.76 g, 1.26 mmol, 71%). TLC (3:1 hexanes–EtOAc): R_f 0.3; $[\alpha]_D$ –31.7° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.65 (d, 1 H, CHO), 7.33–7.16 (m, 12 H, ArH), 6.99 (d, 2 H, ArH), 6.83 (d, 2 H, ArH), 6.80 (d, 2 H, ArH), 5.05 (d, 1 H, $ArCH_2O$), 4.84 (m, 3 H, $ArCH_2O$, H-1, $J_{H1,\ H2}$ = 10.0 Hz), 4.56 (d, 1 H, $ArCH_2O$), 4.40 (dd, 2 H, $ArCH_2O$), 4.00 (t, 1 H, H-3), 3.74 (s, 3 H, OCH_3), 3.72 (s, 3 H, OCH_3), 3.81–3.67 (m, 2 H, H-5, H-3), 3.58 (m, 2 H, H-6), 3.01 (t, 1 H, H-4); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 200.1, 159.4, 155.5, 151.4, 138.3, 138.0, 129.8, 129.5, 128.5, 128.5, 128.3, 128.1, 127.9, 118.5, 114.7, 113.9, 102.8, 82.6, 78.8, 75.2, 75.1, 73.2, 72.1, 70.3, 57.3, 55.7, 55.3; ESIMS (positive-ion mode): *m/z* 621.1 $[M + Na]^+$, 637.2 $[M + K]^+$. Anal. Calcd for $C_{36}H_{38}O_8$ (598.70): C, 72.22; H, 6.40. Found: C, 72.44; H, 6.28. The data match those reported in Kenneth Price's dissertation.[66]

2-Pyridinyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (77). To a solution of compound **76** (20.0 g, 45.5 mmol) in MeOH (150 mL) and CH_2Cl_2 (30 mL) was added NaOMe (25% in MeOH, 1.0 mL). The reaction was stirred at r. t. for 1 h, after which time 1 mL of satd NH_4Cl solution was added, and the solvent was evaporated to afford

compound **77** (13.6 g, 43.2 mmol, 95%) as a white amorphous solid that was used in the next step without characterization. mp 154–156 °C; $[\alpha]_D$ +9.5° (*c* 1.0, DMSO).

2-Pyridinyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-1-thio-*β*-D-glucopyranoside (**78**). Compound **77** (16.0 g, 51.0 mmol) was stirred with dry $ZnCl_2$ (14 g, 0.10 mol) in benzaldehyde (100 mL) at r. t. for 16 h, after which time the reaction was quenched with water (250 mL). The suspension was filtered, and the solid was washed with MeOH and EtOAc sequentially to afford compound **78** as a white amorphous solid (16.3 g, 40.5 mmol, 80%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.4; mp 164–166 °C; $[\alpha]_D$ +4.6° (*c* 0.5, DMSO); ^{1}H NMR (250 MHz, DMSO-d_6): δ 8.43–7.12 (m, 4 H, ArH), 7.47–7.32 (m, 5 H, ArH), 5.62 (s, 1 H, PhCH), 5.54 (d, 1 H, H-1, $J_{H1, H2}$ = 10.5 Hz), 5.46 (d, 1 H, NH), 4.19–4.17 (m, 1 H, H-6), 3.85 (dd, 1 H, H-2), 3.74–3.63 (m, 2 H, H-3, H-4), 3.59–3.48 (m, 2 H, H-6, H-5), 3.16 (d, 1 H, OH), 1.80 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, DMSO-d_6): 169.2, 157.2, 149.4, 137.7, 137.2, 128.9, 128.0, 126.4, 122.0, 120.5, 100.7, 83.3, 81.0, 71.7, 70.2, 67.6, 54.0, 23.0; ESIMS (positive-ion mode): *m/z* 403.1 $[M + H]^+$, 425.1 $[M + Na]^+$, 441.1 $[M + K]^+$. Anal. Calcd for $C_{20}H_{22}N_2O_5S \cdot 0.16CH_2Cl_2$ (416.06): C, 58.20; H, 5.41; N, 6.73. Found: C, 58.19; H, 5.56; N, 6.50. (The CH_2Cl_2 of solvation was confirmed by NMR spectroscopy.)

2-Pyridinyl 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-1-thio-*β*-D-glucopyranoside (**79**). To a solution of compound **78** (16.30 g, 40.54 mmol) and imidazole (6.25g, 96.0 mmol) in dry DMF was added *tert*-butyldimethylsilyl chloride

(10.43 g, 69.0 mmol) at 0 °C. The reaction was allowed to stir and warm to r. t. over 15 h, after which time it was quenched with water, washed with satd $NaHCO_3$, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (2.5:1 to 1:1 hexanes–EtOAc) to yield compound **79** as a pale-yellow solid (16.3 g, 31.6 mmol, 78%). TLC (1:2 hexanes–EtOAc): R_f 0.5; mp 210–212 °C; $[\alpha]_D$ +4.3° (*c* 1.0, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 8.44–7.03 (m, 4 H, ArH), 7.55–7.34 (m, 5 H, ArH), 5.98 (d, 1 H, NH), 5.85 (d, 1 H, H-1, $J_{H1,\ H2}$ = 10.6 Hz), 5.51 (s, 1 H, PhCH), 4.31 (dd, 1 H, H-6), 4.20–3.96 (m, 2 H, H-2, H-3), 3.82–3.48 (m, 3 H, H-6, H-5, H-4), 1.91 (s, 3 H, CH_3CO), 0.82 (s, 9 H, $C(CH_3)_3$), 0.05 (s, 3 H, $SiCH_3$), –0.02 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.1, 156.6, 149.4, 137.2, 136.6, 129.0, 128.1, 126.3, 123.5, 120.6, 101.8, 83.2, 82.1, 74.0, 70.8, 68.7, 56.2, 25.6, 23.5, 18.1, –4.1, –5.0; ESIMS (positive-ion mode): *m/z* 517.2 $[M + H]^+$, 539.2 $[M + Na]^+$, 555.2 $[M + K]^+$. Anal. Calcd for $C_{26}H_{36}N_2O_5SSi$ (516.74): C, 60.43; H, 7.02; N, 5.42. Found: C, 60.41; H, 6.83; N, 5.36.

2-Acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose (**20**). To a stirred solution of compound **79** (16.3 g, 31.6 mmol) in CH_2Cl_2 (200 mL) was added *m*-CPBA (50–60%, 33.0 g) at 0 °C. The reaction was allowed to stir and warm to r. t. over 1.5 h, after which time the reaction mixture was diluted with CH_2Cl_2, washed consecutively with satd $Na_2S_2O_3$, satd Na_2CO_3 and brine, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4

and then concentrated to dryness. The residue was submitted to silica gel column chromatography (1:1 hexanes–EtOAc) to give compound **20** as a white amorphous solid (13.9 g, 25.4 mmol, 79%). TLC (1:2 hexanes–EtOAc): R_f 0.4; mp 162–164 °C; $[\alpha]_D$ – 34.8° (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.85 (d, 1 H, ArH), 8.16 (d, 1 H, ArH), 8.02 (t, 1 H, ArH), 7.62 (t, 1 H, ArH), 7.50–7.39 (m, 5 H, ArH), 6.84 (d, 1 H, NH), 5.81 (d, 1 H, H-1, $J_{H1,H2}$ = 10.3 Hz), 4.72–4.61 (m, 1 H, H-6), 4.12–4.02 (m, 2 H, H-2, H-3), 3.69–3.48 (m, 3 H, H-6, H-5, H-4), 2.06 (s, 3 H, CH_3CO), 0.09 (s, 9 H, $C(CH_3)_3$), 0.06 (s, 3 H, $SiCH_3$), –0.01 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.0, 155.1, 150.2, 137.8, 136.8, 128.9, 127.9, 127.6, 126.1, 124.2, 101.7, 86.1, 81.6, 71.0, 70.1, 67.9, 53.5, 25.6, 23.5, 17.9, –4.4, –5.1; ESIMS (positive-ion mode): *m/z* 549.0 $[M + H]^+$, 571.0 $[M + Na]^+$, 587.0 $[M + K]^+$. Anal. Calcd for $C_{26}H_{36}N_2O_7SSi$ (548.74): C, 56.91; H, 6.61; N, 5.11. Found: C, 56.72; H, 6.60; N, 4.96.

Samarium diiodide–promoted coupling reaction—Preparation of 80a, 80b, and 80c. To a stirred solution of sulfone **20** (2.90 g, 5.3 mmol) and aldehyde **21** (2.50 g, 4.2 mmol) in THF (50 mL) was added a solution of SmI_2 in dry THF (0.1 M, 150 mL, 15 mmol) at 20 °C under N_2. The reaction was stirred at r. t. for 1 h, after which time it was quenched with satd NH_4Cl and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4, and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 to 1:1 hexanes–EtOAc) to afford **80a** (845 mg, 0.84 mmol,

20%), **80b** (1.25g, 1.24 mmol, 30%) and **80c** (630 mg, 0.63 mmol, 15%) as white amorphous solids.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (80a)**. TLC (2:1 hexanes–EtOAc): R_f 0.4; mp 176–178 °C; $[\alpha]_D$ –41.2° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51–7.19 (m, 17 H, ArH), 7.07 (d, 2 H, ArH), 6.84 (d, 2 H, ArH), 6.75 (d, 2 H, ArH), 5.44 (s, 1 H, PhCH), 5.07 (d, 1 H, $ArCH_2O$), 4.99 (d, 1 H, $ArCH_2O$), 4.99 (d, 1 H, NH), 4.91 (d, 1 H, H-1^I, $J_{H1,H2}$ = 7.2 Hz), 4.80 (d, 1 H, $ArCH_2O$), 4.59 (d, 1 H, $ArCH_2O$), 4.45 (dd, 2 H, $ArCH_2O$), 4.21 (dd, 1 H, H-6^{II}), 4.02 (s, 1 H, CH-O**H**), 3.97 (dd, 1 H, H-6^I), 3.91–3.83 (m, 2 H, H-5^I, H-2^{II}), 3.80–3.76 (m, 3 H, H-2^I, H-3^I, C**H**-OH), 3.78 (s, 3 H, CH_3O), 3.76 (s, 3 H, CH_3O), 3.62–3.57 (m, 2 H, H-6^I, H-6^{II}), 3.43–3.36 (m, 2 H, H-4^{II}, H-1^{II}, $J_{H1,H2}$= 8.4 Hz), 3.29–3.21 (m, 2 H, H-3^{II}, H-5^{II}), 2.32–2.26 (m, 1 H, H-4^I), 1.76 (s, 3 H, CH_3CO), 0.77 (s, 9 H, $C(CH_3)_3$), –0.05 (s, 3 H, $SiCH_3$), –0.08 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.2, 158.9, 155.0, 151.5, 138.8, 138.1, 137.1, 130.8, 129.8, 129.0, 128.6, 128.4, 128.1, 127.8, 127.7, 126.2, 118.2, 114.5, 113.6, 102.7, 101.8, 83.1, 82.0, 78.5, 78.4, 74.6, 74.2, 73.7, 73.5, 72.8, 71.4, 70.5, 68.6, 67.3, 55.5, 55.1, 53.5, 46.0, 25.6, 23.2, 18.0, –4.0, –4.9; ESIMS (positive-ion mode): *m/z* 1028.4 $[M + Na]^+$, 1044.5 $[M + K]^+$. Anal. Calcd for $C_{57}H_{71}NO_{13}Si$ (1006.28): C, 68.04; H, 7.11; N, 1.39. Found: C, 67.76; H, 7.22; N, 1.34.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (80b)**. TLC (1:2 hexanes–EtOAc): R_f 0.5; mp 90–92 °C; $[\alpha]_D$ –97.1° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47–7.24 (m, 17 H, ArH), 7.04 (d, 2 H, ArH), 6.87 (d, 2 H, ArH), 6.79 (d, 2 H, ArH), 5.40 (s, 1 H, PhCH), 5.09 (d, 1 H, $ArCH_2O$), 5.03 (d, 1 H, $ArCH_2O$), 4.99 (d, 1 H, NH), 4.94 (d, 1 H, H-1^I, $J_{H1, H2}$ = 6.6 Hz), 4.77 (d, 1 H, $ArCH_2O$), 4.65 (d, 1 H, $ArCH_2O$), 4.50 (d, 1 H, $ArCH_2O$), 4.43 (d, 1 H, $ArCH_2O$), 4.17 (dd, 1 H, H-6^{II}), 3.88–3.74 (m, 5 H, H-5^I, H-3^{II}, H-2^I, C**H**-OH, H-3^I), 3.78 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 3.72 (dd, 1 H, H-6^I), 3.61 (dd, 1 H, H-6^I), 3.58-3.52 (m, 2 H, H-6^{II}, H-1^{II}, $J_{H1, H2}$ = 9.6 Hz), 3.48 (dd, 1 H, H-2^{II}), 3.28 (t, 1 H, H-4^{II}), 3.26–3.21 (m, 1 H, H-5^{II}), 2.25–2.08 (m, 1 H, H-4^I), 1.89 (s, 3 H, CH_3CO), 0.08 (s, 9 H, $C(CH_3)_3$), –0.03 (s, 3 H, $SiCH_3$), –0.07 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.8, 159.3, 155.1, 151.4, 138.5, 138.0, 137.2, 130.0, 129.7, 129.0, 128.7, 128.4, 128.1, 128.1, 127.8, 127.7, 126.3, 126.2, 114.5, 113.8, 102.8, 101.7, 83.2, 82.2, 79.5, 78.7, 74.4, 73.1, 72.9, 71.5, 71.5, 69.6, 68.6, 56.9, 55.6, 55.2, 45.3, 25.7, 23.5, 18.1, –4.1, –5.0; ESIMS (positive-ion mode): *m/z* 1006.4 [M + H$^+$], 1028.5 [M + Na]$^+$, 1044.6 [M + K]$^+$. Anal. Calcd for $C_{57}H_{71}NO_{13}Si$ (1006.28): C, 68.04; H, 7.11; N, 1.39. Found: C, 67.74; H, 6.95; N, 1.38.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-**

methoxybenzyl-4a-carba-α-D-glucopyranoside (**80c**). TLC (2:1 hexanes–EtOAc): R_f 0.2; mp 96–98 °C; $[\alpha]_D$ –2.9° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47–7.26 (m, 15 H, ArH), 7.21 (d, 2 H, ArH), 7.00 (d, 2 H, ArH), 6.84 (d, 2 H, ArH), 6.81 (d, 2 H, ArH), 6.10 (d, 1 H, NH), 5.44 (s, 1 H, PhCH), 5.11 (d, 1 H, $ArCH_2O$), 5.05 (d, 1 H, $ArCH_2O$), 4.93 (d, 1 H, H-1^I, $J_{H1,H2}$ = 7.2 Hz), 4.75 (d, 1 H, $ArCH_2O$), 4.74 (d, 1 H, $ArCH_2O$), 4.46 (d, 1 H, $ArCH_2O$), 4.35 (d, 1 H, $ArCH_2O$), 4.27 (m, 1 H, H-2^{II}) 4.12 (dd, 1 H, H-6^{II}), 4.02 (m, 1 H, H-4^{II}), 3.95 (m, 2 H, H-3^I, H-3^{II}), 3.84–3.71 (m, 4 H, H-6^I, H-5^I, H-1^{II}, C**H**-OH), 3.78 (s, 3 H, CH_3O), 3.78 (s, 3 H, CH_3O), 3.68 (t, 1 H, H-2^I), 3.65–3.61 (m, 1 H, H-6^I), 3.56 (t, 1 H, H-6^{II}), 3.50–3.40 (m, 1 H, H-5^{II}), 2.05–1.98 (m, 1 H, H-4^I), 1.86 (s, 3 H, CH_3CO), 0.75 (s, 9 H, $C(CH_3)_3$), –0.08 (s, 3 H, $SiCH_3$), –0.13 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 169.7, 159.1, 155.1, 150.9, 137.5, 137.3, 137.1, 129.6, 129.0, 128.8, 128.6, 128.3, 128.1, 128.1, 128.0, 127.7, 127.7, 126.1, 118.2, 114.4, 113.5, 102.5, 101.6, 83.0, 82.7, 80.0, 75.2, 74.3, 73.5, 73.2, 71.9, 71.4, 71.3, 69.1, 67.6, 65.4, 55.6, 55.2, 54.5, 48.3, 25.7, 23.4, 18.0, –4.0, –4.9; ESIMS (positive-ion mode): *m/z* 1006.2 $[M + H]^+$, 1023.2 $[M + NH_4]^+$, 1028.2 $[M + Na]^+$, 1044.2 $[M + K]^+$. Anal. Calcd for $C_{57}H_{71}NO_{13}Si$ (1006.28): C, 68.04; H, 7.11; N, 1.39. Found: C, 67.79; H, 7.03; N, 1.47.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside** (**83a**). To a solution of compound **80a** (1.90 g, 1.68 mmol) and imidazole (10 mg, 0.15 mmol)

in dry THF (15 mL) was added NaH (60% in mineral oil, 135 mg, 3.38 mmol). The reaction was stirred for 30 min, after which time CS_2 (1.74 mL, 3.78 mmol) was added, and then MeI (0.42 mL, 6.72 mmol) was added after another 40 min. The mixture was stirred for 40 min, after which time it was quenched with wet CH_2Cl_2 (20 mL), poured into water (50 mL), and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 to 2:1 hexanes–EtOAc) to yield compound **83a** as a white amorphous solid (1.01 g, 0.91 mmol, 54%). TLC (2:1 hexanes–EtOAc): R_f 0.5; mp 85–87 °C; $[\alpha]_D$ –4.3° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46–7.23 (m, 17 H, ArH), 7.06 (d, 2 H, ArH), 6.85 (d, 2 H, ArH), 6.74 (d, 2 H, ArH), 6.33 (m, 1 H, CHOC=S), 5.44 (s, 1 H, PhCH), 5.09 (d, 1 H, $ArCH_2O$), 5.08 (d, 1 H, $ArCH_2O$), 4.86 (d, 1 H, H-1^I, $J_{H1, H2}$ = 7.8 Hz), 4.75 (d, 1 H, $ArCH_2O$), 4.67 (d, 1 H, $ArCH_2O$), 4.51 (d, 1 H, $ArCH_2O$), 4.42 (d, 1 H, $ArCH_2O$), 4.23 (dd, 1 H, H-6^{II}) 4.00–3.95 (m, 2 H, H-6^I, H-5^I), 3.80–3.74 (m, 1 H, H-2^I), 3.77 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.66–3.32 (m, 8 H, H-3^I, H-6^{II}, H-6^I, H-3^{II}, H-2^{II}, H-1^{II}, H-5^{II}, H-4^{II}), 2.72–2.52 (m, 1 H, H-4^I), 2.55 (s, 3 H, SCH_3), 1.49 (s, 3 H, CH_3CO), 0.77 (s, 9 H, $C(CH_3)_3$), –0.08 (s, 3 H, $SiCH_3$), –0.09 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 216.3, 169.7, 158.9, 155.1, 151.5, 139.0, 138.0, 137.1, 130.8, 129.0, 128.3, 128.0, 127.7, 127.4, 127.3, 126.3, 118.3, 114.4, 113.5, 102.9, 101.9, 83.4, 82.3, 78.9, 75.5, 74.5, 74.3, 73.4, 72.9, 71.8, 71.0, 70.6, 68.5, 55.5, 55.1, 54.5, 44.9, 25.6, 23.3, 19.4, 18.0, –4.2, –5.1; ESIMS (positive-ion mode): *m/z* 1096.4 $[M + H]^+$, 1118.5 $[M + Na]^+$, 1134.6 $[M + K]^+$. Anal. Calcd for $C_{59}H_{73}NO_{13}S_2Si$ (1096.45): C, 64.63; H, 6.71; N, 1.28. Found: C, 64.58; H, 6.71; N, 1.26.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (83b).** To a solution of compound **80b** (1.90 g, 1.68 mmol) and imidazole (10 mg, 0.15 mmol) in dry THF (15 mL) was added NaH (60% in mineral oil, 135 mg, 3.38 mmol). The reaction was stirred for 30 min, after which time CS_2 (1.74 mL, 3.78 mmol) was added, and then MeI (0.42 mL, 6.72 mmol) was added after another 40 min. The mixture was stirred for 40 min, after which time it was quenched with wet CH_2Cl_2 (20 mL), poured into water (50 mL), and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 to 2:1 hexanes–EtOAc) to yield compound **83b** as a white amorphous solid (0.94 g, 0.85 mmol, 50%). TLC (2:1 hexanes–EtOAc): R_f 0.45; mp 80–82 °C; $[\alpha]_D$ –9.0° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46–7.23 (m, 17 H, ArH), 7.11 (d, 2 H, ArH), 6.85 (d, 2 H, ArH), 6.75 (d, 2 H, ArH), 6.42 (m, 1 H, CHOC=S), 5.37 (s, 1 H, PhCH), 5.32 (d, 1 H, $ArCH_2O$), 5.05 (d, 1 H, $ArCH_2O$), 5.00 (d, 1 H, NH), 4.93 (d, 1 H, H-1^I, $J_{H1,H2}$ = 7.2 Hz), 4.78 (dd, 2 H, $ArCH_2O$), 4.58 (t, 1 H, H-4^{II}), 4.48 (dd, 2 H, $ArCH_2O$), 4.43 (d, 1 H, H-1^{II}, $J_{H1,H2}$ = 10.8 Hz), 4.14 (d, 1 H, H-6^{II}), 4.02 (d, 1 H, H-6^I), 3.77 (s, 3 H, CH_3O), 3.76 (s, 3 H, CH_3O), 3.79–3.73 (m, 3 H, H-3^{II}, H-2^I, H-3^I), 3.49–3.43 (m, 4 H, H-5^I, H-1^{II}, H-6^{II}, H-6^I), 3.19 (t, 1 H, H-5^{II}), 2.73 (m, 1 H, H-2^{II}), 2.55 (s, 3 H, SCH_3), 2.21 (t, 1 H, H-4^I), 1.33 (s, 3 H, CH_3CO), 0.79 (s, 9H, $C(CH_3)_3$), –0.11 (s, 3H, $SiCH_3$), –0.14 (s, 3H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$):

δ 216.7, 170.2, 159.1, 155.0, 151.5, 138.8, 137.8, 137.2, 130.6, 129.2, 129.1, 128.9, 128.3, 128.2, 128.0, 127.8, 126.3, 126.2, 118.0, 114.5, 113.7, 102.7, 101.8, 83.1, 82.5, 80.4, 79.1, 76.8, 75.0, 74.3, 73.9, 73.0, 72.3, 69.7, 68.9, 68.3, 56.9, 55.5, 55.1, 42.2, 25.6, 23.4, 19.0, 18.1, –4.3, –5.1; ESIMS (positive-ion mode): *m/z* 1118.1 $[M + Na]^+$, 1134.1 $[M + K]^+$. Anal. Calcd for $C_{59}H_{73}NO_{13}S_2Si$ (1096.45): C, 64.63; H, 6.71; N, 1.28. Found: C, 64.39; H, 6.86; N, 1.22.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (19)**. To a refluxing solution of tri-*n*-butyltin hydride (1.33 mL, 5.0 mmol) in dry toluene (10 mL) was added a solution of compound **83a** or **83b** (1.00 g, 0.91 mmol) and AIBN (11 mg) in dry toluene (10 mL) dropwise. The reaction was stirred for 30 min, and then the reaction mixture was extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and concentrated to dryness. The residue was submitted to coarse silica gel column chromatography (2:1 hexanes–EtOAc) to yield compound **19** as a white amorphous solid (820 mg, 0.83 mmol, 91%). TLC (2:1 hexanes–EtOAc): R_f 0.3; mp 67–69 °C; $[\alpha]_D$ –21.3° (*c* 0.5, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$): δ 7.47–7.25 (m, 20 H, ArH), 7.04 (d, 2 H, ArH), 6.89 (d, 2 H, ArH), 6.80 (d, 2 H, ArH), 5.44 (s, 1 H, PhCH), 5.08 (d, 1 H, $ArCH_2O$), 5.02 (d, 1 H, $ArCH_2O$), 4.84 (d, 1 H, H-1^I, $J_{H1,H2}$ = 7.8 Hz), 4.79 (d, 1 H, $ArCH_2O$), 4.60 (d, 1 H, $ArCH_2O$), 4.57 (d, 1 H, NH), 4.51 (d, 1 H, $ArCH_2O$), 4.44 (d, 1 H, $ArCH_2O$), 4.19 (dd, 1 H, H-6^{II}), 3.79 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.74–3.68 (m, 3 H, H-6^I, H-2^I, H-3^{II}), 3.60–3.50 (m, 4 H, H-6^I, H-6^{II}, H-2^{II}, H-3^I),

3.50–3.44 (m, 2 H, H-5^{I}, H-4^{II}), 3.34–3.28 (m, 1 H, H-1^{II}, $J_{H1,H2}$ = 8.4 Hz), 3.25–3.20 (m, 1 H, H-5^{II}), 2.12–2.05 (m, 1 H, H-4^{I}), 1.73 (m, 1 H, CH_2), 1.67 (s, 3 H, CH_3CO), 1.61 (dd, 1 H, CH_2), 0.77 (s, 9 H, $C(CH_3)_3$), –0.03 (s, 3 H, $SiCH_3$), –0.08 (s, 3 H, $SiCH_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 169.5, 159.1, 155.1, 151.5, 139.1, 138.1, 137.1, 130.2, 129.5, 128.9, 128.4, 128.3, 128.1, 128.0, 127.5, 126.2, 118.3, 114.4, 113.7, 103.0, 101.7, 83.2, 82.4, 80.7, 75.8, 74.5, 73.8, 73.3, 73.0, 70.0, 68.7, 57.0, 55.4, 55.1, 39.8, 28.8, 25.5, 23.3, 17.9, –4.1, –5.1; ESIMS (positive-ion mode): *m/z* 1012.4 $[M + Na]^+$, 1028.5 $[M + K]^+$. Anal. Calcd for $C_{57}H_{71}NO_{12}Si$ (990.28): C, 69.13; H, 7.23; N, 1.41. Found: C, 68.57; H, 7.28; N, 1.34.

***p*-Methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (84).** To a solution of compound **19** (1.22 g, 1.23 mmol) in dry THF (20 mL) was added Bu_4NF (1.35 mL, 1.0 M in THF, 1.1 equiv). The reaction was stirred at r. t. for 1.5 h, after which time it was quenched with water, and the mixture was extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (50:1 CH_2Cl_2–MeOH) to give compound **84** as a white amorphous solid (1.00 g, 1.14 mmol, 93%). TLC (10:1 CH_2Cl_2–MeOH): R_f 0.5; mp 234–236 °C; $[\alpha]_D$ –36.7° (*c* 0.5, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$): δ 7.53–7.24 (m, 15 H, ArH), 7.21 (d, 2 H, ArH), 7.04 (d, 2 H, ArH), 6.82 (dd, 4 H, ArH), 6.67 (d, 1 H, NH), 5.52 (s, 1 H, PhCH), 5.16 (d, 1 H, $ArCH_2O$), 5.11 (d, 1 H, $ArCH_2O$), 4.90 (d, 1 H, H-1^{I}, $J_{H1,H2}$ = 7.8 Hz), 4.89 (d, 1 H, $ArCH_2O$), 4.60 (d, 1 H,

$ArCH_2O$), 4.48 (s, 2 H, $ArCH_2O$), 4.29–4.24 (m, 1 H, H-6^I), 4.16–4.13 (dd, 1 H, H-6^{II}), 3.90–3.87 (m, 1 H, H-5^I), 3.79 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.70–3.67 (m, 2 H, H-2^I, H-3^{II}), 3.64–3.60 (m, 1 H, H-6^I), 3.54 (dd, 1 H, H-3^I), 3.47–3.34 (m, 5 H, H-6^{II}, H-5^{II}, H-1^{II}, H-2^{II}, H-4^{II}), 2.04–1.98 (m, 1 H, H-4^I), 1.81–1.76 (m, 1 H, CH_2), 1.57 (s, 3 H, $COCH_3$), 1.39–1.36 (m, 1 H, CH_2); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.4, 159.2, 155.3, 151.3, 137.9, 137.2, 136.8, 129.8, 129.4, 129.3, 129.1, 129.0, 128.8, 128.5, 128.3, 128.2, 127.9, 126.3, 118.4, 114.5, 113.7, 102.9, 101.7, 83.1, 83.0, 82.7, 76.8, 74.5, 74.0, 73.2, 70.1, 69.1, 69.0, 64.8, 55.6, 55.2, 53.5, 41.6, 28.9, 22.5; ESIMS (positive-ion mode): *m/z* 876.3 $[M + H]^+$, 893.3 $[M + NH_4]^+$, 898.2 $[M + Na]^+$, 914.3 $[M + K]^+$. Anal. Calcd for $C_{51}H_{57}NO_{12}$ (876.01): C, 69.93; H, 6.56; N, 1.60. Found: C, 69.86; H, 6.66; N, 1.67.

Allyl 2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranoside (98). To a solution of glycosyl bromide **97** (45.0 g, 109.8mmol) and allyl alcohol (13.0 mL, 0.64 mol) in dry $CHCl_3$ (150 mL) were added $HgBr_2$ (4.5 g, 12.5 mmol), HgO (24.0 g, 110 mmol), and $CaSO_4$ (46.2 g, 340 mmol) at 0 °C. The reaction was allowed to stir and warm to r. t. over 10 h, after which time it was filted, washed with aq NaBr, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 hexanes–EtOAc) to give pure **98** as a colorless syrup (41.73 g, 107.6 mmol, 98%). TLC (1:1 hexanes–EtOAc): R_f 0.78. The data match those reported in the literature.[94]

Allyl β-D-galactopyranoside (99). To a solution of compound **98** (30.0 g, 66.1 mmol) in dry CH_2Cl_2 (50 mL) and MeOH (250 mL) was added NaOMe (25% in MeOH, 0.25 mL). The reaction was stirred at r. t. for 1 h, after which time Dowex 50 × 2-100 (H^+ form) was added to quench the reaction. The suspension was filtered and evaporated to afford tetraol **99** as a white amorphous solid (18.2 g, 63.6 mmol, 96%) that was used in the next step without characterization. TLC (5:1 CH_2Cl_2–MeOH): R_f 0.55.

Allyl 4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (100). To a solution of allyl β-D-galactopyranoside (**99**) (17.0 g, 77.3 mmol) and *p*-toluenesulfonic acid monohydrate (TsOH) (0.5 g, 2.6 mmol) in dry acetonitrile (200 mL) was added anisaldehyde dimethyl acetal (ADMA) (22.55 mL, 115.9 mmol, 1.5 equiv). The solution was stirred at r. t. for 3 h, after which time triethylamine (TEA) was added to quench the reaction, and the suspension was filtered. The solid was washed with EtOAc and MeOH sequentially to afford compound **100** as a white amorphous solid (23.0 g, 68.0 mmol, 88%). TLC (5:1 CH_2Cl_2–acetone): R_f 0.35; mp 183–184 °C; $[\alpha]_D$ –23.5° (*c* 1.0, DMSO); ^{1}H NMR (250 MHz, DMSO-d_6): δ 7.36 (d, 2 H, ArH), 6.91 (d, 2 H, ArH), 5.89 (m, 1 H, C**H**=CH_2), 5.36 (s, 1 H, CH_3OPhCH), 5.34 (dd, 1 H, CH=C**H**$_2$), 5.14 (dd, 1 H, CH=C**H**$_2$), 5.03 (d, 1 H, H-2), 4.89 (d, 1 H, H-3), 4.25 (m, 1 H, OC**H**$_2$CH=CH_2), 4.23 (d, 1 H, H-1, $J_{H1, H2}$ = 7.5 Hz), 4.06 (m, 1 H, OC**H**$_2$CH=CH_2), 4.03 (m, 3 H, H-5, H-6), 3.74 (s, 3 H, OCH_3), 3.43 (s, 2 H, OH), 3.39 (s, 1 H, H-4); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 159.35, 134.91, 131.05, 127.54, 116.48, 113.16, 102.42, 99.68, 75.92, 71.91, 70.00, 68.88, 68.52, 65.90, 55.09; ESIMS (positive-ion mode): *m/z* 339.1 $[M + H]^+$, 356.0 $[M + NH_4]^+$, 361.1 $[M + Na]^+$,

377.1 $[M + K]^+$. Anal. Calcd for $C_{17}H_{22}O_7$ (338.36): C, 60.35; H, 6.55. Found: C, 60.20; H, 6.65.

Allyl 2,3-di-*O*-acetyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (101). To a solution of allyl 4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**100**) (5.0 g, 14.8 mmol) in dry pyridine (6.0 mL, 74.2 mmol) was added Ac_2O (5.0 mL, 45.3 mmol). The reaction was stirred at r. t. for 10 h, after which time it was quenched with water, and the solution was sequentially washed with aq $NaHCO_3$ and 1 M HCl and then extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and evaporated to dryness. The residue was crystallized from EtOAc and hexanes to give pure **101** as colorless crystals (5.68 g, 13.5 mmol, 91%). TLC (2:1 hexanes–EtOAc): R_f 0.41; mp 156–157 °C; $[\alpha]_D$ +51.8° (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 7.44 (d, 2 H, ArH), 6.89 (d, 2 H, ArH), 5.85 (m, 1 H, C**H**=CH_2), 5.45 (s, 1 H, CH_3OPhCH), 5.38 (dd, 1 H, CH=C**H**$_2$), 5.27 (dd, 1 H, CH=C**H**$_2$), 5.17 (d, 1 H, H-2), 4.96 (d, 1 H, H-3), 4.54 (d, 1 H, H-1, $J_{H1,H2}$ = 7.5 Hz), 4.39 (m, 1 H, OC**H**$_2$CH=CH_2), 4.34 (dd, 2 H, H-6), 4.12 (m, 1 H, OC**H**$_2$CH=CH_2), 4.04 (d, 1 H, H-5), 3.80 (s, 3 H, OCH_3), 3.48 (s, 1 H, H-4), 2.07 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.46, 169.13, 159.94, 133.65, 130.01, 127.54, 116.86, 113.31, 100.74, 99.73, 73.22, 71.80, 69.17, 68.63, 68.48, 66.13, 55.08, 20.64; ESIMS (positive-ion mode): *m/z* 439.9 $[M + NH_4]^+$, 444.9 $[M + Na]^+$, 460.8 $[M + K]^+$. Anal. Calcd for $C_{21}H_{26}O_9$ (422.43): C, 59.71; H, 6.20. Found: C, 59.68; H, 6.21.

Allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (102). To a mixture of allyl 2,3-di-*O*-acetyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**101**) (4.26 g, 10.1 mmol), $NaBH_3CN$ (2.54 g, 40.4 mmol), and 4Å MS (2.0 g) in dry DMF (30 mL) was added trifluoroacetic acid (TFA) (5.78 mL, 80.8 mmol) dropwise at 0 °C. The reaction was then allowed to stir and warm to r. t. over 10 h, after which time it was filtered through a Celite bed. The mixture was neutralized with satd $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 hexanes–EtOAc) to give pure **102** as a colorless syrup (3.90 g, 9.2 mmol, 91%). TLC (1:1 hexanes–EtOAc): R_f 0.32; $[\alpha]_D$ –5.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.24 (d, 2 H, ArH), 6.86 (d, 2 H, ArH), 5.85 (m, 1 H, C**H**=CH_2), 5.29 (dd, 1 H, H-2), 5.23 (dd, 1 H, CH=C**H**$_2$), 5.15 (dd, 1 H, CH=C**H**$_2$), 4.92 (d, 1 H, H-3), 4.88 (d, 1 H, H-1, $J_{H1,H2}$ = 9.4 Hz), 4.86 (s, 2 H, ArCH_2O), 4.32 (dd, 1 H, O**CH**$_2$CH=CH_2), 4.07 (m, 2 H, O**CH**$_2$CH=CH_2, H-6), 3.77 (s, 3 H, OCH_3), 3.71 (m, 3 H, H-6, H-5, H-4), 3.12 (s, 1 H, OH), 2.06 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.13, 169.36, 159.02, 133.52, 129.61, 129.16, 116.85, 113.63, 99.90, 73.35, 73.06, 69.37, 69.20, 68.57, 67.54, 55.00, 20.57; ESIMS (positive-ion mode): *m/z* 442.2 $[M + NH_4]^+$, 446.9 $[M + Na]^+$, 462.9 $[M + K]^+$. Anal. Calcd for $C_{21}H_{28}O_9$ (424.44): C, 59.43; H, 6.65. Found: C, 59.03; H, 6.77.

Allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-*O*-trifluoromethanesulfonyl-β-D-galactopyranoside (58). To a solution of allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-β-

D-galactopyranoside (**102**) (4.25 g, 10.0 mmol) and dry pyridine (2.64 mL, 32.0 mmol) in dry CH_2Cl_2 was added triflic anhydride (2.73 mL, 16.0 mmol) dropwise at 0 °C. The reaction was stirred at 0 °C for 10 h, after which time it was concentrated to dryness. The residue was passed though a short plug of silica gel (2.5:1 hexanes–EtOAc) to give pure **58** as an unstable, pale-yellow syrup (5.28 g, 9.5 mmol, 95%) that was used in the next step without characterization. TLC (2:1 hexanes–EtOAc): R_f 0.49.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (56). To a 100-mL flask containing 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-*β*-D-glucopyranose (**35**) (705 mg, 1.94 mmol, 1.2 equiv) and NaH (60% in mineral oil, 93 mg, 2.33 mmol, 1.2 equiv) under N_2 was added dry DMF (20 mL) at 0 °C. The mixture was stirred for 10 min, and then a solution of triflate **58** (900 mg, 1.62 mmol) in dry DMF (10 mL) was added. The reaction was allowed to stir at 0 °C for 4 h, after which time it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (1:2 hexanes–EtOAc) to afford compound **56** as a white amorphous solid (635 mg, 0.83 mmol, 51%). TLC (1:3 hexanes–EtOAc): R_f 0.38; mp 68–69 °C; $[\alpha]_D$ –34.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 (d, 2 H, ArH), 6.90 (d, 2 H, ArH), 5.82 (m, 1 H, C**H**=CH_2), 5.52 (d, 1 H, NH), 5.23 (dd, 1 H, CH=C**H**$_2$), 5.16 (dd, 1 H, CH=C**H**$_2$), 5.10 (dd, 1 H, H-3^I), 4.98 (t, 1 H, H-2^I), 4.95 (m, 2 H, H-3^{II}, H-4^{II}), 4.65

(d, 1 H, H-1^{II}, $J_{H1, H2}$ = 10.8 Hz), 4.56 (d, 1 H, $ArCH_2O$), 4.43 (d, 1 H, $ArCH_2O$), 4.41 (d, 1 H, H-1^{I}, $J_{H1, H2}$ = 8.4 Hz), 4.31 (m, 1 H, $OCH_2CH=CH_2$), 4.06 (m, 4 H, H-2^{II}, H-6^{II}, $OCH_2CH=CH_2$), 3.94 (dd, 1 H, H-6^{I}), 3.81 (m, 1 H, H-6^{I}), 3.79 (s, 3 H, OCH_3), 3.67 (dd, 1 H, H-5^{I}), 3.55 (m, 1 H, H-5^{II}), 3.01 (t, 1 H, H-4^{I}), 2.04 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.98 (s, 3 H, CH_3CO), 1.85 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.05, 170.50, 170.04, 169.41, 169.06, 169.01, 159.09, 133.40, 129.94, 129.28, 116.85, 113.63, 99.41, 82.19, 75.48, 75.27, 74.03, 73.07, 72.30, 70.54, 69.27, 68.52, 68.23, 62.38, 55.02, 52.19, 45.79, 22.71, 20.65, 20.35; ESIMS (positive-ion mode): *m/z* 770.1 $[M + H]^+$, 787.1 $[M + NH_4]^+$, 792.0 $[M + Na]^+$, 808.0 $[M + K]^+$. Anal. Calcd for $C_{35}H_{47}NO_{16}S$ (769.83): C, 54.61; H, 6.15; N, 1.82. Found: C, 54.33; H, 6.15; N, 1.85.

Allyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (104). To a solution of triflate **58** (1.27g, 2.28 mmol) in dry DMF (10 mL) was added potassium thioacetate (520 mg, 4.56 mmol, 2 equiv) at 0 °C. The reaction was stirred at 0 °C for another 1 h, after which time it was diluted with EtOAc, washed with water, and extracted with EtOAc. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 hexanes–EtOAc) to give pure **104** as a white amorphous solid (0.84g, 1.73 mmol, 76%). TLC (2:1 hexanes–EtOAc): R_f 0.31; mp 102–103 °C; $[\alpha]_D$ – 23.6° (*c* 0.5, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 7.25 (d, 2 H, ArH), 6.87 (d, 2 H, ArH), 5.84 (m, 1 H, $CH=CH_2$), 5.23 (m, 3 H, H-2, $CH=CH_2$), 4.97 (d, 1 H, H-3), 4.54 (d,

1 H, H-1, $J_{H1, H2}$ = 8.03 Hz), 4.47 (s, 2 H, $ArCH_2O$), 4.34 (dd, 1 H, $OCH_2CH=CH_2$), 4.10 (dd, 2 H, $OCH_2CH=CH_2$, H-6), 3.73 (m, 1 H, H-6), 3.72 (s, 3 H, OCH_3), 3.67 (m, 2 H, H-6, H-5), 3.57 (t, 1 H, H-4), 2.28 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 192.91, 169.85, 169.16, 159.00, 133.38, 129.83, 129.10, 117.03, 113.49, 99.14, 74.12, 72.93, 72.60, 71.20, 69.45, 69.14, 54.99, 44.52, 30.45, 20.44, 20.33; ESIMS (positive-ion mode): *m/z* 500.0 $[M + NH_4]^+$, 504.9 $[M + Na]^+$, 520.8 $[M + K]^+$. Anal. Calcd for $C_{23}H_{30}O_9S$ (482.16): C, 57.25; H, 6.27. Found: C, 57.51; H, 6.39.

Allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (105). To a solution of cysteamine (431 mg, 3.80 mmol, 4 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (284 μL, 1.90 mmol, 2 equiv) in dry DMF (10 mL) was added allyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (**104**) (420 mg, 0.95 mmol) at 0 °C. The reaction was stirred at 0 °C for 1 h, after which time it was diluted with EtOAc, washed with water, and extracted with EtOAc. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 to 2:1 hexanes–EtOAc) to give pure **105** as a colorless syrup (393 mg, 0.89 mmol, 94%). TLC (2:1 hexanes–EtOAc): R_f 0.30; $[\alpha]_D$ – 52.4° (*c* 0.5, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 7.28 (d, 2 H, ArH), 6.89 (d, 2 H, ArH), 5.85 (m, 1 H, $CH=CH_2$), 5.21 (m, 2 H, $CH=CH_2$), 4.94 (m, 2 H, H-2, H-3), 4.60 (d, 1 H, $ArCH_2O$), 4.51 (d, 1 H, H-1, $J_{H1, H2}$ = 6.55 Hz), 4.47 (d, 1 H, $ArCH_2O$), 4.31 (dd, 1 H, $OCH_2CH=CH_2$), 4.09 (dd, 1 H, $OCH_2CH=CH_2$), 3.84 (m, 2 H, H-6), 3.80 (s, 3 H,

OCH_3), 3.45 (m, 1 H, H-5), 3.06 (dd, 1 H, H-4), 2.09 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 1.40 (d, 1 H, SH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.28, 169.37, 159.18, 133.50, 129.92, 129.28, 117.14, 113.69, 99.47, 77.57, 75.27, 73.10, 72.48, 69.56, 68.87, 55.13, 40.30, 20.58; ESIMS (positive-ion mode): *m/z* 458.2 $[M + NH_4]^+$, 463.2 $[M + Na]^+$, 479.2 $[M + K]^+$. Anal. Calcd for $C_{23}H_{30}O_9S$ (440.15): C, 57.26; H, 6.41. Found: C, 57.50; H, 6.54.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (56) (Route 2). To a solution of allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (**105**) (393 mg, 0.89 mmol) in dry DMF (10 mL) was added K_2CO_3 (185 mg, 1.31 mmol) at 0 °C. The mixture was stirred for 10 min, and then a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**75**) (975 mg, 2.67 mmol, 3 equiv) in dry DMF (10 mL) was added. The reaction was stirred for 2 h at 0 °C, after which time it was quenched with water and extracted with EtOAc. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (1:2 hexanes–EtOAc) to afford compound **56** as white amorphous solid (593 mg, 0.77 mmol, 86%). The data of this compound match those of the compound synthesized using NaH as the promoter.

***S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α, β-D-glucopyranose (106).** (1,5-

cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (100 mg) was suspended in dry tetrahydrofuran (THF) (5 mL) at r. t. and treated with H_2 for 15 min until the solids had completely dissolved and the red color had completely changed to a pale tan color. Then the solution was evacuated, purged with N_2 and added to a 50-mL flask containing compound **56** (1.5 g, 1.95 mmol) under N_2. The reaction was stirred at r. t. for 3 days, after which time it was cooled down to 0 °C and a solution of $NaHCO_3$ (620.5 mg, 7.38 mmol) in water (15 mL) and I_2 (1.48 g, 5.85 mmol) were added. The reaction was stirred at 0 °C for another 20 min, then it was diluted with water and CH_2Cl_2. Solid sodium thiosulfate was added until the iodine color completely disappeared. The mixture was extracted with CH_2Cl_2, and the organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (60:1 CH_2Cl_2–MeOH) to afford compound **106**, with an α, β anomeric ratio of 1:2, as a white amorphous solid (1.351 g, 1.85 mmol, 95%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.53; $[\alpha]_D$ –5.2° (*c* 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.27 (d, 2 H, β-ArH), 7.25 (d, 1 H, α-ArH), 6.91 (d, 2 H, β-ArH), 6.89 (d, 1 H, α-ArH), 5.72 (d, 0.5 H, α-NH), 5.53 (m, 1.5 H, β-NH, α-H-3^I), 5.49 (t, 0.5 H, α-H-1^I, $J_{H1,\,H2}$ = 3.0 Hz, $J_{H1,\,OH}$ = 3.6 Hz), 5.16 (dd, 1 H, β-H-3^I), 5.02 (dd, 1.5 H, β-H-4^{II}, α-H-4^{II}), 4.99 (m, 0.5 H, α-H-2^I), 4.85 (t, 1 H, β-H-2^I), 4.78 (d, 0.5 H, α-H-1^{II}, $J_{H1,\,H2}$ = 10.8 Hz), 4.69 (d, 1 H, β-H-1^{II}, $J_{H1,\,H2}$ =10.2 Hz), 4.58 (dd, 1 H, β-H-1^I, $J_{H1,\,H2}$ = 9 Hz, $J_{H1,\,OH}$ = 8.4 Hz,), 4.57 (d, 1 H, β- $ArCH_2O$), 4.54 (d, 0.5 H, α-$ArCH_2O$), 4.45 (d, 1.5 H, α-$ArCH_2O$, β-$ArCH_2O$), 4.16–4.05 (m, 4.5 H, β-H-2^{II}, α-H-2^{II}, β-H-3^{II}, α-H-3^{II}, β-H-6^{II}, α-H-6^{II}), 3.98 (m, 1.5 H,

β-H-6^{I}, α-H-6^{I}), 3.82 (s, 4.5 H, α-CH_3O, β-CH_3O), 3.81–3.73 (m, 3 H, β-H-6^{I}, α-H-6^{I}, β-H-5^{I}, α-H-5^{I}), 3.63 (m, 0.5 H, α-H-5^{II}), 3.60 (m, 1 H, β-H-5^{II}), 3.11 (t, 1 H, β-H-4^{I}), 3.09 (t, 0.5 H, α-H-4^{I}), 2.10 (s, 3 H, β-CH_3CO), 2.09 (s, 1.5 H, α-CH_3CO), 2.08 (s, 3 H, β-CH_3CO), 2.04 (s, 3 H, β-CH_3CO), 2.03 (s, 3 H, α-CH_3CO), 2.02 (s, 1.5 H, α-CH_3CO), 2.01 (s, 3 H, β-CH_3CO), 1.91 (s, 1.5 H, α-CH_3CO), 1.88 (s, 3 H, β-CH_3CO), 1.61 (s, 1.5 H, α-CH_3CO), 1.60 (s, 3 H, β-CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.34, 171.22, 170.76, 170.68, 170.58, 170.40, 169.98, 169.83, 169.76, 169.26, 159.27, 159.15, 129.83, 129.73, 129.49, 113.82, 113.70, 95.10, 89.95, 82.02, 81.89, 76.99, 76.48, 75.32, 74.38, 74.12, 73.31, 72.45, 70.01, 69.66, 68.64, 68.14, 67.40, 62.42, 62.26, 60.32, 55.19, 52.10, 45.75, 22.81, 20.67, 20.51; ESIMS (positive-ion mode): *m/z* 730.1 $[M + H]^+$, 752.0 $[M + Na]^+$, 768.1 $[M + K]^+$. Anal. Calcd for $C_{32}H_{43}NO_{16}S$ (729.76): C, 52.67; H, 5.94; N, 1.92. Found: C, 52.43; H, 6.01; N, 1.93.

_S_-(2-Acetamido-3,4,6-tri-_O_-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-_O_-acetyl-6-_O_-_p_-methoxybenzyl-4-thio-α, β-D-glucopyranosyl trichloroacetimidate (54). To a mixture of compound **106** (103 mg, 0.14 mmol) and trichloroacetonitrile (0.14 mL, 14 mmol, 10 equiv) in dry CH_2Cl_2 (2 mL) was added 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) (1 drop). The reaction was stirred at r. t. for 40 min, after which time it was concentrated to dryness and submitted to coarse silica gel column chromatography (1:2.5 hexanes–EtOAc) to afford compound **54**, with an α, β anomeric ratio of 6:1, as an unstable colorless foam (104 mg, 0.12 mmol, 86%). TLC (1:3 hexanes–EtOAc): R_f 0.43

(α anomer); $[\alpha]_D$ +19.0° (*c* 1.0, $CHCl_3$, α anomer); ^1H NMR (600 MHz, $CDCl_3$, α anomer): δ 8.63 (s, 1 H, C=NH), 7.26 (d, 2 H, ArH), 6.90 (d, 2 H, ArH), 6.61 (d, 1 H, H-1^I, $J_{H1,H2}$ = 3.6 Hz), 5.70 (d, 1 H, NH), 5.55 (dd, 1 H, H-3^I), 5.11 (dd, 1 H, H-2^I), 5.00 (m, 2 H, H-3^{II}, H-4^{II}), 4.70 (d, 1 H, H-1^{II}, $J_{H1,H2}$ = 10.8 Hz), 4.54 (d, 1 H, $ArCH_2O$), 4.46 (d, 1 H, $ArCH_2O$), 4.31 (d, 1 H, H-5^I), 4.18 (m, 1 H, H-2^{II}), 4.11 (d, 1 H, H-6^I), 4.05 (m, 2 H, H-6^{II}), 3.82 (s, 3 H, OCH_3), 3.67 (dd, 1 H, H-6^I), 3.53 (m, 1 H, H-5^{II}), 3.25 (t, 1 H, H-4^I), 2.09 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 1.98 (s, 3 H, CH_3CO), 1.91 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$, α anomer): δ 171.28, 170.80, 170.22, 169.68, 169.53, 169.17, 160.73, 159.30, 129.86, 129.52, 113.80, 94.12, 82.02, 75.51, 74.40, 73.45, 71.09, 68.16, 66.03, 67.00, 62.32, 55.22, 51.93, 45.07, 22.92, 20.96, 20.55; ESIMS (positive-ion mode): *m/z* 890.1 $[M + NH_4]^+$, 895.0 $[M + Na]^+$, 911.0 $[M + K]^+$. Anal. Calcd for $C_{34}H_{43}Cl_3N_2O_{16}S$ (874.14): C, 46.72; H, 4.96; N, 3.20. Found: C, 46.86; H, 5.02; N, 3.07.

Allyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (107). To a solution of allyl 4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**100**) (6.50 g, 19.20 mmol) in dry DMF was added NaH (60% in mineral oil, 2.3 g, 57.5 mmol) at 0 °C. After stirring for 10 min, BnBr (5.5 mL, 46.3 mmol) was added dropwise. The reaction was allowed to stir and warm to r. t. over 10 h, after which time it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then concentrated to dryness. The residue was submitted to coarse silica gel column chromatography (2:1 hexanes–EtOAc) to give pure **107** as a white amorphous solid (9.2

g, 17.76 mmol, 93%). TLC (2:1 hexanes–EtOAc): R_f 0.71; mp 125–126 °C; $[\alpha]_D$ +29.3° (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 7.49–7.24 (m, 12 H, ArH), 6.87 (d, 2 H, ArH), 5.91 (m, 1 H, C**H**=CH_2), 5.44 (s, 1 H, CH_3OPhCH), 5.33 (dd, 1 H, CH=C**H**$_2$), 5.18 (dd, 1 H, CH=C**H**$_2$), 4.94 (d, 1 H, $ArCH_2O$), 4.77 (d, 1 H, $ArCH_2O$), 4.75 (m, 2 H, H-2, H-3), 4.46 (m, 1 H, OC**H**$_2$CH=CH_2), 4.43 (d, 1 H, H-1, $J_{H1, H2}$ = 7.5 Hz), 4.28 (d, 1 H, $ArCH_2O$), 4.13 (m, 1 H, OC**H**$_2$CH=CH_2), 4.09 (m, 1 H, H-6), 3.98 (d, 1 H, $ArCH_2O$), 3.87 (t, 1 H, H-5), 3.79 (s, 3 H, OCH_3), 3.54 (dd, 1 H, H-6), 3.28 (s, 1 H, H-4); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 160.00, 138.84, 138.45, 134.22, 130.49, 128.43, 128.25, 128.19, 128.04, 127.89, 127.76, 127.66, 127.55, 127.44, 117.05, 113.42, 102.63, 101.17, 79.21, 78.43, 75.24, 73.90, 71.92, 70.10, 69.12, 66.35, 55.23; ESIMS (positive-ion mode): *m/z* 519.1 $[M + H]^+$, 541.1 $[M + Na]^+$, 557.0 $[M + K]^+$. Anal. Calcd for $C_{31}H_{34}O_7$ (518.61): C, 71.80; H, 6.61. Found: C, 71.65; H, 6.62.

Allyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (108). To a mixture of allyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**107**) (6.07 g, 11.73 mmol), $NaBH_3CN$ (2.95 g, 46.92 mmol), and 4Å MS (2.0 g) in dry DMF (30 mL) was added trifluoroacetic acid (TFA) (6.71 mL, 94.64 mmol) dropwise at 0 °C. The reaction was allowed to stir and warm to r. t. over 10 h, after which time it was filtered through a Celite bed. The mixture was neutralized with satd $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (3:1 hexanes–EtOAc) to give pure **108** as a colorless syrup (3.89 g, 7.66

mmol, 65%). TLC (2:1 hexanes–EtOAc): R_f 0.70; $[\alpha]_D$ +7.6° (*c* 0.5, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 7.35–7.24 (m, 12 H, ArH), 6.87 (d, 2 H, ArH), 5.94 (m, 1 H, C**H**=CH_2), 5.33 (dd, 1 H, CH=C**H**$_2$), 5.18 (dd, 1 H, CH=C**H**$_2$), 4.92 (d, 1 H, $ArCH_2O$), 4.72 (d, 1 H, $ArCH_2O$), 4.71 (s, 2 H, $ArCH_2O$), 4.50 (s, 2 H, $ArCH_2O$), 4.43 (m, 1 H, O**CH**$_2$CH=CH_2), 4.40 (d, 1 H, H-1, $J_{H1, H2}$ = 7.5 Hz), 4.12 (m, 1 H, O**CH**$_2$CH=CH_2), 4.00 (d, 1 H, H-4), 3.79 (s, 3 H, OCH_3), 3.76–3.64 (m, 3 H, H-2, H-3, H-6), 3.55–3.45 (m, 2 H, H-5, H-6), 2.40 (s, 1 H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 159.21, 138.50, 137.83, 134.01, 129.99, 129.31, 128.33, 128.17, 128.04, 127.71, 127.49, 116.99, 113.73, 102.63, 80.51, 78.88, 75.11, 73.24, 73.09, 72.29, 70.00, 68.76, 66.78, 55.15; ESIMS (positive-ion mode): *m/z* 521.1 $[M + H]^+$, 538.1 $[M + NH_4]^+$, 543.1 $[M + Na]^+$, 559.1 $[M + K]^+$, 1063.1 $[2M + Na]^+$. Anal. Calcd for $C_{31}H_{36}O_7$ (520.62): C, 71.52; H, 6.97. Found: C, 71.46; H, 6.99.

Allyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-*O*-trifluoromethanesulfonyl-β-D-galactopyranoside (59). To a solution of allyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (**108**) (3.89 g, 7.66 mmol) and dry pyridine (1.45 mL, 17.58 mmol) in dry CH_2Cl_2 (20 mL) was added triflic anhydride (1.50 mL, 8.79 mmol) dropwise at 0 °C. The reaction was stirred at 0 °C for 10 h, after which time it was concentrated to dryness and passed though a short plug of coarse silica gel (2.5:1 hexanes–EtOAc) to give pure **59** as an unstable, pale-yellow syrup (4.69 g, 92%) that was used in the next step without characterization. TLC (2:1 hexanes–EtOAc): R_f 0.75.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (57). To a 100-mL flask containing 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranose (**35**) (3.33 g, 9.17 mmol, 1.2 equiv) and NaH (60% in mineral oil, 0.44 g, 11.0 mmol, 1.2 equiv) was added dry DMF (20 mL) at 0 °C under N_2. The mixture was stirred for 10 min, and then a solution of triflate **59** (4.99 g, 7.66 mmol) in dry DMF (10 mL) was added. The reaction was stirred at 0 °C for 4 h, after which time it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (1:2 hexanes–EtOAc) to afford compound **57** as a white amorphous solid (4.95 g, 5.72 mmol, 75%). TLC (1:2 hexanes–EtOAc): R_f 0.40; mp 197–198 °C; $[\alpha]_D$ +33.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (d, 2 H, ArH), 7.33–7.25 (m, 10 H, ArH), 6.92 (d, 2 H, ArH), 5.97 (m, 1 H, C**H**=CH_2), 5.35 (dd, 1 H, CH=C**H**$_2$), 5.21 (dd, 1 H, CH=C**H**$_2$), 5.08 (m, 2 H, H-3^{II}, NH), 4.94 (m, 3 H, H-4^{II}, $ArCH_2O$), 4.83 (d, 1 H, $ArCH_2O$), 4.76 (d, 1 H, H-1^{II}, $J_{H1,H2}$ = 10.2 Hz), 4.71 (d, 1 H, $ArCH_2O$), 4.63 (d, 1 H, $ArCH_2O$), 4.47 (d, 1 H, $ArCH_2O$), 4.43 (m, 1 H, OC**H**$_2$CH=CH_2), 4.40 (d, 1 H, H-1^I, $J_{H1,H2}$ = 7.8 Hz), 4.15 (m, 1 H, OC**H**$_2$CH=CH_2), 4.10 (dd, 1 H, H-6^I), 3.92 (m, 1 H, H-6^I), 3.89 (m, 1 H, H-6^{II}), 3.84 (d, 1 H, H-6^{II}), 3.81 (s, 3 H, OCH_3), 3.76 (dd, 1 H, H-2^{II}), 3.49 (m, 2 H, H-2^I, H-3^I), 3.40 (m, 2 H, H-5^I, H-5^{II}), 2.97 (t, 1 H, H-4^I), 2.01 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.99 (s, 3 H, CH_3CO), 1.65 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.43, 169.89, 169.28, 159.27, 138.65, 138.14, 133.95, 130.19, 129.49, 128.24, 128.13, 127.61, 127.56, 127.31, 117.15, 113.85, 102.47, 82.92, 82.77, 80.69, 77.00, 76.49, 76.24, 75.31,

74.85, 74.76, 73.20, 73.09, 70.03, 69.48, 68.33, 62.12, 55.15, 54.14, 46.46, 22.89, 20.55; ESIMS (positive-ion mode): *m/z* 866.1 $[M + H]^+$, 883.1 $[M + NH_4]^+$, 888.0 $[M + Na]^+$, 904.0 $[M + K]^+$. Anal. Calcd for $C_{45}H_{55}NO_{14}S$ (865.99): C, 62.41; H, 6.40; N, 1.62. Found: C, 62.25; H, 6.41; N, 1.59.

Allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (55). To a solution of compound **57** (6.0 g, 6.94 mmol) in dry CH_2Cl_2 (10 mL) and MeOH (50 mL) was added NaOMe (25% in MeOH, 0.2 mL). The reaction was allowed to stir at r. t. for 2 h, after which time it was neutralized with Dowex 50 × 2-100 (H^+ form), filtered, and concentrated to dryness to afford the triol as a white amorphous solid. To a suspension of the triol thus obtained in dry acetonitrile (100 mL) was added *p*-toluenesulfonic acid monohydrate (0.1 g) and benzaldehyde dimethyl acetal (1.56 mL, 10.4 mmol, 1.5 equiv). The solution was stirred at r. t. for 3 h, after which time it was quenched with triethylamine (TEA). The suspension was filtered, and the solid was washed with EtOAc and MeOH sequentially to afford acceptor **55** as a white amorphous solid (5.33 g, 6.45 mmol, 93%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.51; mp 213–214 °C; $[\alpha]_D$ –25.1° (*c* 1.0, DMSO); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47–7.25 (m, 17 H, ArH), 6.92 (d, 2 H, ArH), 5.95 (m, 2 H, NH, C**H**=CH_2), 5.47 (s, 1 H, PhCH), 5.35 (dd, 1 H, CH=C**H**$_2$), 5.22 (dd, 1 H, CH=C**H**$_2$), 4.94 (d, 1 H, $ArCH_2O$), 4.89 (s, 2 H, $ArCH_2O$), 4.72 (d, 1 H, $ArCH_2O$), 4.59 (d, 1 H, H-1^{II}, $J_{H1,H2}$ = 10.2 Hz), 4.51 (d, 1 H, $ArCH_2O$), 4.42 (dd, 1 H, O**CH**$_2$CH=CH_2), 4.39 (d, 1 H, H-1^{I}, $J_{H1,H2}$ = 7.8 Hz), 4.16 (dd, 1 H, O**CH**$_2$CH=CH_2),

4.06 (dd, 1 H, H-6^{I}), 4.03 (dd, 1 H, H-6^{II}), 3.84 (d, 1 H, H-6^{I}), 3.77 (s, 3 H, OCH_3), 3.63 (m, 2 H, H-2^{II}, H-3^{II}), 3.54 (t, 1 H, H-6^{II}), 3.49 (t, 1 H, H-2^{I}), 3.45 (m, 2 H, H-4^{II}, H-5^{I}), 3.40 (t, 1 H, H-3^{I}), 3.17 (m, 1 H, H-5^{II}), 3.00 (t, 1 H, H-4^{I}), 1.81 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 169.01, 158.63, 139.00, 138.64, 137.76, 134.70, 130.60, 128.79, 128.14, 128.02, 127.96, 127.66, 127.39, 126.40, 116.31, 113.59, 101.57, 100.72, 83.32, 82.89, 81.04, 80.07, 75.04, 74.55, 73.87, 71.83, 71.49, 69.48, 69.09, 55.33, 54.99, 46.76, 22.98; ESIMS (positive-ion mode): *m/z* 828.2 $[M + H]^+$, 850.2 $[M + Na]^+$, 866.1 $[M + K]^+$. Anal. Calcd for $C_{46}H_{53}NO_{11}S$ (828.00): C, 66.73; H, 6.45; N, 1.69. Found: C, 66.48; H, 6.47; N, 1.68.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (53). To a suspension of acceptor **55** (708.7 mg, 0.86 mmol, 1.1 equiv) and 4Å MS (0.5 g) in dry CH_2Cl_2 was added TMSOTf (0.01 M in CH_2Cl_2, 1.55 mL) at –15 °C under N_2. The mixture was stirred for 10 min, and then a solution of trichloroacetimidate **54** (670 mg, 0.78 mmol) in dry CH_2Cl_2 was added. The reaction was allowed to stir at –15 °C under N_2 for another 2 h, after which time it was quenched with triethylamine (TEA), filtered, and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (2:1 CH_2Cl_2–EtOAc) to afford tetrasacchride **53** as a white amorphous solid (690 mg, 0.45 mmol, 58%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.55; mp 206–207 °C; $[\alpha]_D$ –18° (*c* 0.1,

$CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.43–7.26 (m, 17 H, ArH), 7.22 (d, 2H, ArH), 6.91(dd, 4 H, ArH), 5.97 (m, 1 H, C**H**=CH_2), 5.44 (d, 1 H, NH^{IV}), 5.41 (s, 1 H, PhCH), 5.35 (m, 2 H, CH=C**H**$_2$, NH^{II}), 5.21 (dd, 1 H, CH=C**H**$_2$), 4.97 (m, 3 H, H-1^{II}, H-3^{II}, H-4^{IV}), 4.93 (d, 1 H, $ArCH_2O$), 4.87 (m, 4 H, H-2^{III}, H-3^{IV}, $ArCH_2O$), 4.69 (d, 1 H, $ArCH_2O$), 4.66 (d, 1 H, $ArCH_2O$), 4.58 (d, 1 H, H-1^{III}, $J_{H1, H2}$ = 6.6 Hz), 4.52 (d, 1 H, H-1^{IV}, $J_{H1, H2}$ = 10.8 Hz), 4.47 (d, 1 H, $ArCH_2O$), 4.40 (m, 3 H, $ArCH_2O$, H-1^{I}, $J_{H1, H2}$ = 7.8 Hz), 4.15 (m, 4 H, OC**H**$_2$CH=CH_2, H-6^{II}, H-2^{II}, H-3^{II}), 4.02 (m, 2 H, H-2^{IV}, H-6^{IV}), 3.84 (m, 2 H, H-6^{I}, H-6^{IV}), 3.80 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.73 (m, 2 H, H-6^{III}), 3.59 (t, 1 H, H-4^{II}), 3.48 (m, 5 H, H-6^{II}, H-2^{I}, H-6^{I}, H-5^{III}, H-5^{I}), 3.34 (t, 1 H, H-3^{I}), 3.28 (m, 2 H, H-5^{IV}, H-5^{II}), 3.04 (t, 1 H, H-4^{I}), 2.89 (t, 1 H, H-4^{III}), 2.04 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.89 (s, 3 H, CH_3CO), 1.84 (s, 3 H, CH_3CO), 1.70 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.92, 170.71, 170.49, 169.85, 169.49, 169.37, 169.07, 159.31, 159.03, 138.65, 138.20, 137.27, 133.91, 130.28, 129.91, 129.82, 128.98, 128.18, 128.06, 127.56, 127.42, 127.16, 126.21, 117.18, 113.80, 102.39, 101.30, 99.11, 83.47, 83.27, 82.88, 81.40, 79.33, 77.51, 76.49, 75.49, 75.48, 75.18, 74.83, 74.03, 73.18, 73.09, 72.65, 71.19, 70.05, 69.97, 69.07, 68.44, 67.85, 61.81, 55.80, 55.15, 52.37, 46.43, 46.10, 23.15, 22.81, 20.62, 20.45; ESIMS (positive-ion mode): *m/z* 1539.2 $[M + H]^+$, 1556.3 $[M + NH_4]^+$, 1561.2 $[M + Na]^+$, 1577.1 $[M + K]^+$. Anal. Calcd for $C_{78}H_{94}N_2O_{26}S_2$ (1539.72): C, 60.85; H, 6.15; N, 1.56. Found: C, 60.63; H, 6.10; N, 1.76.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-β-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-4-thio-β-D-glucopyranoside (109). To a solution of tetrasaccharide **53** (170 mg, 0.11 mmol) in CH_2Cl_2 (15 mL) and H_2O (1 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (74.9 mg, 0.33 mmol, 3 equiv). The reaction was stirred at r. t. for 1 h, after which time the mixture was poured into a satd $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (40:1 CH_2Cl_2–MeOH) to afford compound **109** as a white amorphous solid (85 mg, 0.065 mmol, 60%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.48; mp 245–246 °C; $[\alpha]_D$ +5.4° (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.35–7.24 (m, 15H, ArH), 5.92 (m, 1 H, C**H**=CH_2), 5.63 (s, 1 H, PhCH), 5.31 (dd, 1 H, CH=C**H**$_2$), 5.15 (dd, 1 H, CH=C**H**$_2$), 5.04 (m, 2 H, H-3^{III}, H-4^{IV}), 4.84 (d, 1 H, $ArCH_2O$), 4.79 (m, 6 H, H-1^{II}, H-2^{III}, H-1^{IV}, $ArCH_2O$, NH^{IV}), 4.72 (d, 1 H, $ArCH_2O$), 4.63 (m, 3 H, H-1^{III}, $J_{H1,H2}$ = 9.6 Hz, H-3^{IV}, $ArCH_2O$), 4.45 (d, 1 H, H-1^{I}, $J_{H1,H2}$ = 7.8 Hz), 4.42 (br-s, 1 H, NH^{II}), 4.34 (dd, 1 H, OC**H**$_2$CH=CH_2), 4.15 (dd, 1 H, H-6^{II}), 4.09 (dd, 1 H, OC**H**$_2$CH=CH_2), 3.97 (m, 2 H, H-6^{II}, H-6^{IV}), 3.80 (m, 2 H, H-6^{III}, H-2^{IV}), 3.69 (m, 4 H, H-6^{III}, H-6^{I}, H-3^{II}, H-2^{II}), 3.60 (m, 3 H, H-3^{I}, H-6^{IV}, H-5^{III}), 3.55 (m, 1 H, H-5^{I}), 3.38 (dd, 1 H, H-6^{I}), 3.25 (m, 3 H, H-2^{I}, H-5^{IV}, H-5^{II}), 3.14 (t, 1 H, H-4^{II}), 2.95 (t, 1 H, H-4^{III}), 2.69 (t, 1 H, H-4^{I}), 2.00 (s, 3 H, CH_3CO), 1.95 (s, 3 H, CH_3CO), 1.92 (s, 3 H, CH_3CO), 1.91 (s, 3 H, CH_3CO), 1.89 (s, 3 H, CH_3CO), 1.73 (s, 3 H, CH_3CO), 1.57 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 170.76, 170.48, 170.40, 169.99, 169.89, 169.76, 169.43,

139.58, 139.32, 135.30, 130.18, 129.85, 128.84, 128.71, 128.34, 128.16, 128.02, 117.06, 102.21, 100.81, 99.88, 84.79, 83.77, 83.59, 81.05, 80.67, 80.10, 79.66, 79.21, 77.14, 76.88, 75.16, 74.96, 74.52, 74.08, 72.90, 72.35, 69.58, 69.19, 62.76, 62.25, 62.02, 61.19, 53.05, 47.34, 45.85, 23.56, 23.26, 21.17, 21.12, 21.02; ESIMS (positive-ion mode): *m/z* 1299.1 $[M + H]^+$, 1316.0 $[M + NH_4]^+$, 1321.0 $[M + Na]^+$, 1337.0 $[M + K]^+$. Anal. Calcd for $C_{62}H_{78}N_2O_{24}S_2$ (1299.43): C, 57.31; H, 6.05; N, 2.16. Found: C, 57.23; H, 6.02; N, 2.25.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-β-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-4-thio-β-D-glucopyranosiduronic acid (110). To a solution of tetrasacchride **109** (200 mg, 0.154 mmol) in dry DMF (2.0 mL) was added pyridinium dichromate (PDC) (1.16 g, 3.08 mmol, 20 equiv). The reaction was allowed to stir at r. t. for 2 days, after which time it was concentrated to dryness. The residue was submitted to coarse silica gel column chromatography (20:1:1 CH_2Cl_2–MeOH–AcOH) to afford compound **110** as a white amorphous solid (162 mg, 0.122 mmol, 79%). TLC (12:1:1 $CHCl_3$–MeOH–AcOH): R_f 0.39; mp 214–216 °C; $[\alpha]_D$ –50.8° (*c* 0.25, DMSO); ^{1}H NMR (600 MHz, 5:1 $CDCl_3$–CD_3OD): δ 7.48 (d, 2 H, ArH), 7.39–7.28 (m, 13 H, ArH), 5.93 (m, 1 H, C**H**=CH_2), 5.50 (s, 1 H, PhCH), 5.34 (d, 1 H, CH=C**H**$_2$), 5.22 (d, 1 H, CH=C**H**$_2$), 5.15 (t, 1 H, H-3^{IV}), 4.99 (t, 1 H, H-4^{IV}), 4.96 (dd, 1 H, H-3^{III}), 4.93 (d, 2 H, $ArCH_2O$), 4.90 (d, 2 H, $ArCH_2O$), 4.89 (t, 1 H, H-2^{III}), 4.81 (d, 2 H, $ArCH_2O$), 4.76 (d, 1 H, H-1^{III}, $J_{H1, H2}$ =

7.8 Hz), 4.71 (d, 1 H, H-1^{II}, $J_{H1, H2}$ = 7.2 Hz), 4.69 (d, 2 H, $ArCH_2O$, H-1^{IV}, $J_{H1, H2}$ = 11.4 Hz), 4.49 (d, 1 H, H-1^{I}, $J_{H1, H2}$ = 7.8 Hz), 4.41 (dd, 1 H, $OCH_2CH{=}CH_2$), 4.23 (dd, 1 H, H-6^{IV}), 4.14 (dd, 1 H, $OCH_2CH{=}CH_2$), 4.10 (m, 2 H, H-6^{II}, H-6^{IV}), 4.01 (m, 1 H, H-3^{II}), 3.91 (d, 1 H, H-5^{I}), 3.90 (m, 2 H, H-2^{IV}, H-2^{II}), 3.88 (d, 1 H, H-5^{III}), 3.70 (m, 1 H, H-5^{IV}), 3.61 (m, 2 H, H-5^{II}, H-6^{II}), 3.48 (t, 1 H, H-2^{I}), 3.40 (t, 1 H, H-3^{I}), 3.33 (m, 1 H, H-4^{II}), 3.15 (t, 2 H, H-4^{I}, H-4^{III}), 2.09 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 2.01 (s, 6 H, CH_3CO), 1.96 (s, 3 H, CH_3CO), 1.89 (s, 3 H, CH_3CO); ^{13}C NMR (150 MHz, 5:1 $CDCl_3$–CD_3OD): δ 173.98, 171.41, 170.95, 170.74, 170.60, 169.92, 169.56, 169.28, 138.24, 137.90, 136.98, 133.39, 128.64, 128.14, 127.93, 127.49, 127.42, 125.93, 117.42, 102.65, 100.63, 100.24, 86.51, 85.30, 82.40, 81.00, 78.80, 78.14, 76.40, 75.90, 75.72, 75.19, 74.92, 73.34, 72.38, 71.14, 70.24, 70.16, 68.25, 61.96, 54.39, 52.80, 48.10, 46.70, 22.50, 22.20, 20.26; ESIMS (negative-ion mode): *m/z* 662.3 $[M - 2H]^{2-}$, 1325.3 $[M - H]^{-}$, 1347.3 $[M - 2H + Na]^{-}$, 1363.3 $[M - 2H + K]^{-}$. Anal. Calcd for $C_{62}H_{74}N_2O_{26}S_2$ (1327.38): C, 56.10; H, 5.62; N, 2.11. Found: C, 55.87; H, 5.83; N, 2.01.

***n*-Propyl *S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-(4-thio-β-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-4-thio-β-D-glucopyranosiduronic acid (52).** To a solution of compound **110** (40 mg, 0.03 mmol) in AcOH (2 mL) and H_2O (0.5 mL) was added Pd/C (10%, 100 mg). The reaction was stirred for 72 h in a H_2 atmosphere (50 Psi), after which time the mixture was filtered though a pad of Celite, which was then washed with MeOH. [Caution. Extreme fire hazard.] The combined filtrates were concentrated to give a white

amorphous solid. TLC (5:1:1 $CHCl_3$–MeOH–AcOH): R_f 0.12; ESIMS (negative-ion mode): *m/z* 529.2 $[M - 2H]^{2-}$, 1059.1 $[M - H]^-$, 1081.1 $[M - 2H + Na]^-$, 1097.1 $[M - 2H + K]^-$. The residue was redissolved in MeOH (2 mL) and treated with NaOMe (25% in MeOH, 2 drops) at r. t. for 2 h. After which time the reaction was neutralized with Dowex 50 × 2-100 (H^+ form), filtered, and concentrated to dryness. The residue was purified by Diaion HP 20 column chromatography (20 cm) with water as an eluent to afford compound **52** as a white amorphous solid (8 mg, 0.009 mmol, 31%). TLC (2:1:1 $CHCl_3$–MeOH–AcOH): R_f 0.25; ^1H NMR (600 MHz, D_2O): δ 4.58 (t, 2 H, H-1^{II}, H-1^{IV}, $J_{H1, H2}$ = 9.6 Hz, 10.2 Hz), 4.43 (t, 2 H, H-1^{I}, H-1^{III}, $J_{H1, H2}$ = 10.2 Hz, 8.4 Hz), 3.91–3.78 (m, 5 H, H-5^{I}, H-5^{III}, H-6^{II}, H-6^{IV}, $OCH_2CH_2CH_3$), 3.75–3.67 (m, 5 H, $OCH_2CH_2CH_3$, H-2^{II}, H-2^{IV}, H-5^{II}, H-5^{IV}), 3.58 (m, 2 H, H-6^{II}, H-6^{IV}), 3.49 (t, 2 H, H-4^{II}, H-4^{IV}), 3.41 (m, 4 H, H-3^{II}, H-3^{IV}, H-3^{I}, H-3^{III}), 3.32 (m, 2 H, H-2^{I}, H-2^{III}), 2.94 (t, 2 H, H-4^{I}, H-4^{III}), 2.00 (s, 3 H, $COCH_3$), 1.97 (s, 3 H, $COCH_3$), 1.58 (m, 2 H, $OCH_2CH_2CH_3$), 0.87 (m, 3 H, $OCH_2CH_2CH_3$); ESIMS (negative-ion mode): *m/z* 848.9 $[M - H]^-$, 870.9 $[M - 2H + Na]^-$, 886.9 $[M - 2H + K]^-$.

Allyl 2,3-di-*O*-benzoyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (111). To a solution of allyl 4,6-O-*p*-methoxybenzylidene-β-D-galactopyranoside (**100**) (3.70 g, 10.9 mmol) in dry pyridine (6.0 mL, 74.2 mmol) was added benzoyl chloride (5 mL, 43.8 mmol) at 0 °C. The reaction was allowed to stir and warm to r. t. over 10 h, after which time it was quenched with water and the solution was extracted with CH_2Cl_2. The organic

phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (2:1 hexanes–EtOAc) to give compound **111** as a white amorphous solid (5.27 g, 9.65 mmol, 89%). TLC (1:1 hexanes–EtOAc): R_f 0.71; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.98 (d, 4 H, ArH), 7.43 (m, 8 H, ArH), 6.88 (d, 2 H, ArH), 5.85 (m, 2 H, H-2, C**H**=CH_2), 5.50 (s, 1 H, CH_3OPhCH), 5.35 (dd, 1 H, H-3), 5.23 (dd, 1 H, CH=C**H**$_2$), 5.11 (dd, 1 H, CH=C**H**$_2$), 4.80 (d, 1 H, H-1, $J_{H1, H2}$ = 8.1 Hz), 4.57 (dd, 1 H, OC**H**$_2$CH=CH_2), 4.39 (m, 2 H, H-6, OC**H**$_2$CH=CH_2), 4.12 (m, 2 H, H-6, H-5), 3.80 (s, 3 H, OCH_3), 3.66 (s, 1 H, H-4); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.21, 165.21, 159.99, 133.71, 133.31, 132.99, 129.92, 129.67, 129.10, 128.34, 128.26, 127.59, 117.40, 113.42, 100.83, 99.81, 76.49, 73.54, 72.81, 69.42, 69.04, 66.87, 66.46, 55.24; ESIMS (positive-ion mode): *m/z* 564.2 $[M + NH_4]^+$, 569.1 $[M + Na]^+$, 585.2 $[M + K]^+$.

Allyl 2,3-di-*O*-benzoyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (112). To a mixture of allyl 2,3-di-*O*-benzoyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**111**) (2.5 g, 4.58 mmol), $NaBH_3CN$ (1.42 g, 22.9 mmol), and 4Å MS (2.0 g) in dry DMF (10 mL) was added trifluoroacetic acid (TFA) (3.28 mL, 45.8 mmol) dropwise at 0 °C. The reaction was allowed to stir and warm to r. t. over 10 h, after which time it was filtered through a Celite bed. The mixture was neutralized with a satd $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (2:1 hexanes–EtOAc) to give pure **112** as a colorless syrup (2.0 g, 3.65

mmol, 80%). TLC (1:1 hexanes–EtOAc): R_f 0.68; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.97 (d, 4 H, ArH), 7.35 (m, 8 H, ArH), 6.88 (d, 2 H, ArH), 5.78 (m, 2 H, H-2, C**H**=CH_2), 5.25 (m, 2 H, CH=C**H**$_2$), 5.10 (d, 1 H, H-3), 4.74 (d, 1 H, H-1, $J_{H1, H2}$ = 8.0 Hz), 4.53 (s, 2 H, $ArCH_2O$), 4.36 (m, 3 H, O**C**H_2CH=CH_2, H-6), 4.15 (dd, 1 H, O**C**H_2CH=CH_2), 3.79 (s, 3 H, OCH_3), 2.84 (s, 1 H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 165.85, 165.28, 159.31, 133.59, 133.25, 132.96, 129.79, 129.64, 129.40, 129.11, 128.34, 128.22, 117.36, 113.84, 100.17, 76.48, 74.40, 73.36, 73.27, 69.689, 69.63, 68.87, 68.02, 55.20; ESIMS (positive-ion mode): *m/z* 442.2 $[M + NH_4]^+$, 446.9 $[M + Na]^+$, 462.9 $[M + K]^+$, 1115.2 $[2M + Na]^+$, 1131.2 $[2M + K]^+$.

Allyl 2,3-di-*O*-benzoyl-4-*O*-trifluoromethanesulfonyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (61). To a solution of allyl 2,3-di-*O*-benzoyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (**112**) (2.0 g, 3.65 mmol) and dry pyridine (1.0 mL, 12.3 mmol) in dry CH_2Cl_2 was added triflic anhydride (0.75 mL, 4.4 mmol) dropwise at 0 °C. The reaction was stirred at 0 °C for 10 h, after which time it was concentrated to dryness and passed though a short plug of coarse silica gel (2:1 hexanes–EtOAc) to give pure **61** as an unstable, pale-yellow syrup (2.4 g, 3.53 mmol, 97%) that was used in the next step without characterization. TLC (2:1 hexanes–EtOAc): R_f 0.65.

Allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzoyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (60). To a 100-mL flask

containing 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-*β*-D-glucopyranose (**35**) (2.0 g, 5.5 mmol, 1.2 equiv) and NaH (60% in mineral oil, 285 mg, 6.5 mmol, 1.2 equiv) under N_2 was added dry DMF (20 mL) at 0 °C. The mixture was stirred for 10 min, and then a solution of triflate **61** (2.4 mg, 3.53 mmol) in dry DMF (10 mL) was added. The reaction was stirred at 0 °C for 4 h, after which time it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (1:2 hexanes–EtOAc) to afford compound **60** as a white amorphous solid (1.67 g, 1.87 mmol, 53%). TLC (1:3 hexanes–EtOAc): R_f 0.33; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (m, 4 H, ArH), 7.52 (m, 1 H, ArH), 7.38 (m, 5 H, ArH), 7.30 (d, 2 H, ArH), 6.91 (d, 2 H, ArH), 5.76 (m, 1 H, C**H**=CH$_2$), 5.59 (t, 1 H, H-3^I), 5.46 (d, 1 H, NH), 5.45 (t, 1 H, H-2^I), 5.20 (dd, 1 H, CH=C**H**$_2$), 5.08 (m, 2 H, H-3^{II}, CH=C**H**$_2$), 4.97 (t, 1 H, H-4^{II}), 4.91 (d, 1 H, H-1^{II}, $J_{H1,\,H2}$ = 10.8 Hz), 4.64 (d, 1 H, H-1^I, $J_{H1,\,H2}$ = 7.8 Hz), 4.59 (d, 1 H, ArCH$_2$O), 4.51 (d, 1 H, ArCH$_2$O), 4.3 (m, 1 H, OC**H**$_2$CH=CH$_2$), 4.11 (m, 2 H, H-2^{II}, OC**H**$_2$CH=CH$_2$), 4.04 (ddd, 2 H, H-6^{II}, H-6^I), 3.90 (d, 1 H, H-6^I), 3.87 (dd, 1 H, H-5^I), 3.82 (s, 3 H, OCH$_3$), 3.73 (m, 1 H, H-5^{II}), 3.29 (t, 1 H, H-4^I), 2.04 (s, 3 H, CH$_3$CO), 2.03 (s, 3 H, CH$_3$CO), 1.99 (s, 3 H, CH$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 172.04, 166.08, 165.19, 137.14, 133.34, 133.04, 129.77, 129.59, 129.28, 129.19, 128.87, 128.21, 127.97, 126.24, 117.29, 101.22, 99.62, 85.88, 80.70, 76.48, 73.02, 72.44, 70.08, 69.84, 67.78, 61.44, 55.56, 47.43, 22.87.

Allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzoyl-4-thio-*β*-D-glucopyranoside (115). To a solution of compound **60** (500 mg,

0.56 mmol) in MeOH (20 mL) and CH_2Cl_2 (4 mL) was added HBF_4 in Et_2O (0.1 mL). The reaction was stirred at r. t. for 1 h. When TLC (5:1 $CHCl_3$–MeOH) showed complete consumption of the starting material and formation of a new spot, the reaction was quenched with triethylamine (TEA), and the solvents were evaporated. To a solution of the resulting residue in dry acetonitrile was added *p*-toluenesulfonic acid monohydrate (TsOH) (50 mg, 0.26 mmol) and benzaldehyde dimethyl acetal (0.13 mL, 0.84 mmol, 1.5 equiv). The solution was stirred at r .t. for 3 h, after which time the reaction was quenched with TEA and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (40:1 CH_2Cl_2–MeOH) to afford compound **115** as colorless foam (296 mg, 0.40 mmol, 72%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.32; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (m, 4 H, ArH), 7.51 (m, 2 H, ArH), 7.38 (m, 4 H, ArH), 6.22 (d, 1 H, NH), 5.78 (m, 1 H, C**H**=CH_2), 5.62 (dd, 1 H, H-3^I), 5.52 (s, 1 H, PhCH), 5.44 (t, 1 H, H-2^I), 5.23 (dd, 1 H, CH=C**H**$_2$), 5.13 (d, 1 H, CH=C**H**$_2$), 4.96 (d, 1 H, H-1^{II}, $J_{H1,\,H2}$ = 10.2 Hz), 4.73 (d, 1 H, H-1^I, $J_{H1,\,H2}$ = 7.8 Hz), 4.35 (m, 1 H, OC**H**$_2$CH=CH_2), 4.15 (m, 1 H, OC**H**$_2$CH=CH_2), 4.09 (m, 2 H, H-6^I), 4.02 (m, 1 H, H-6^{II}), 3.84 (m, 2 H, H-3^{II}, H-2^{II}), 3.71 (m, 1 H, H-5^I), 3.56 (m, 3 H, H-4^{II}, H-5^{II}, H-6^{II}), 3.25 (m, 1 H, H-4^I), 1.78 (s, 3 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 172.1, 166.3, 165.2, 137.1, 133.3, 133.1, 129.8, 129.7, 129.2, 129.0, 128.3, 128.1, 126.3, 117.5, 101.4, 99.6, 85.4, 80.8, 76.3, 73.4, 73.0, 72.3, 70.1, 69.9, 55.7, 47.3, 22.9; ESIMS (positive-ion mode): *m/z* 736.3 [M + H]$^+$, 758.3 [M + Na]$^+$, 774.1 [M + K]$^+$, 1493.3 [2M + Na]$^+$, 1509.3 [2M + K]$^+$.

Allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-4-thio-*β*-D-glucopyranoside (116). To a solution of compound **115** (180 mg, 0.25 mmol), triethylamine (0.034 mL, 1.1 equiv), and DMAP (1.2 mg, 0.04 equiv) in dry CH_2Cl_2 (10 mL) was added *tert*-butyldiphenylsilyl chloride (TBDPSCl) (0.14 mL, 0.52 mmol, 2.2 equiv). The reaction was stirred at r. t. for 18 h, and then it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (1:2 hexanes–EtOAc) to afford compound **116** as a colorless foam (205 mg, 0.18 mmol, 85%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (d, 2 H, ArH), 7.94 (d, 2 H, ArH), 7.77 (dd, 4 H, ArH), 7.45 (m, 12 H, ArH), 6.02 (d, 1 H, NH), 5.82 (m, 1 H, C**H**=CH$_2$), 5.63 (t, 1 H, H-3^I), 5.52 (s, 1 H, PhCH), 5.48 (t, 1 H, H-2^I), 5.22 (d, 1 H, CH=C**H**$_2$), 5.13 (d, 1 H, CH=C**H**$_2$), 5.00 (d, 1 H, H-1^{II}, $J_{H1,\,H2}$ = 10.2 Hz), 4.70 (d, 1 H, H-1^I, $J_{H1,\,H2}$ = 7.8 Hz), 4.36 (m, 1 H, OC**H**$_2$CH=CH$_2$), 4.21 (m, 2 H, H-6^I), 4.15 (m, 1 H, OC**H**$_2$CH=CH$_2$), 3.92 (m, 1 H, H-2^{II}), 3.82 (m, 1 H, H-3^{II}), 3.77 (m, 1 H, H-5^I), 3.55 (m, 3 H, H-4^{II}, H-5^{II}, H-6^{II}), 3.34 (t, 1 H, H-4^I), 1.56 (s, 3 H, CH_3CO), 1.09 (s, 9 H, CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.57, 166.97, 165.00, 136.95, 135.65, 135.47, 133.58, 133.45, 133.31, 132.95, 129.74, 129.61, 129.49, 129.19, 128.95, 128.55, 128.31, 128.15, 128.04, 127.61, 127.51, 126.23, 117.10, 101.50, 99.14, 82.16, 80.82, 76.51, 73.89, 73.00, 71.45, 69.78, 69.00, 68.10, 62.96, 55.14, 45.71, 26.66, 22.55, 19.15.

2-Acetamido-3,4,6-tri-*O*-acetyl-1,2-dideoxy-1-ethyldithio-*β*-D-glucopyranose (121). To a solution of pseudothiourea **103** (20.0 g, 45.5 mmol) in MeOH (100.0 mL) and

triethylamine (15.0 mL) was added ethyl disulfide (15.0 mL, 122 mmol). The reaction was stirred at r. t. for 3 h, after which time it was diluted CH_2Cl_2, washed with water, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (70:1 CH_2Cl_2–MeOH) to give compound **121** as a white amorphous solid (13.04 g, 30.8 mmol, 68%). TLC (10:1 CH_2Cl_2–MeOH): R_f 0.62; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.68 (d, 1 H, NH), 5.28 (t, 1 H, H-3), 5.08 (t, 1 H, H-4), 4.71 (d, 1 H, H-1, $J_{H1, H2}$ = 10.5 Hz), 4.18 (m, 3 H, H-2, H-6), 3.74 (m, 1 H, H-5), 2.80 (q, 2 H, SCH_2CH_3), 2.07 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 1.94 (s, 3 H, CH_3CO), 1.30 (t, 3 H, SCH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.23, 170.86, 169.62, 89.69, 76.22, 73.65, 68.52, 62.47, 52.99, 34.17, 23.54, 20.95, 20.88, 14.52. The data match those reported in the literature.[105]

2-Acetamido-1,2-dideoxy-1-ethyldithio-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (123). To a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-1,2-dideoxy-1-ethyldithio-β-D-glucopyranose (**121**) (3.0 g, 7.1 mmol) in dry CH_2Cl_2 (5.0 mL) and MeOH (25.0 mL) was added NaOMe (25% in MeOH, 0.1 mL). The reaction was stirred at r. t. for 2 h, after which time it was neutralized with Dowex 50 × 2-100 (H^+ form), filtered, and concentrated to afford triol **122** as a white amorphous solid. To a suspension of triol **122** and *p*-toluenesulfonic acid monohydrate (0.1 g, 0.53 mmol) in dry acetonitrile (100.0 mL) was added ADMA (1.70 mL, 9.86 mmol). The solution was stirred at r. t. for 3 h, then the suspension was filtered and the solid was washed with EtOAc and MeOH

sequentially to afford compound **123** as a white amorphous solid (2.53 g, 6.45 mmol, 86%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.49; mp 230–231 °C; $[\alpha]_D$ –98.8° (*c* 1.0, DMSO); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, 1 H, NH), 7.32 (d, 2 H, ArH), 6.89 (d, 2 H, ArH), 5.53 (s, 1 H, $CH_3OPhC\mathbf{H}$), 5.40 (d, 1 H, H-4), 4.58 (d, 1 H, H-1, $J_{H1, H2}$ = 10.5 Hz), 4.16 (dd, 1 H, H-6), 3.73 (s, 3 H, CH_3O), 3.59 (m, 3 H, H-2, H-3, H-6), 3.39 (m, 1 H, H-5), 2.73 (q, 2 H, $SC\mathbf{H}_2CH_3$), 1.80 (s, 3 H, CH_3CO), 1.20 (t, 3 H, $SCH_2C\mathbf{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.14, 159.57, 130.04, 127.73, 113.34, 100.66, 90.92, 80.79, 71.49, 70.32, 67.62, 55.15, 54.56, 32.82, 23.04, 14.24; ESIMS (positive-ion mode): *m/z* 416.1 $[M + H]^+$, 438.0 $[M + Na]^+$, 454.0 $[M + K]^+$. Anal. Calcd for $C_{18}H_{25}NO_6S_2$ (415.11): C, 52.03; H, 6.06; N, 3.37. Found: C, 51.80; H, 5.96; N, 3.28.

2-Acetamido-1,2-dideoxy-1-ethyldithio-3-*O*-levulinoyl-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (124). To a solution of 2-acetamido-1,2-dideoxy-1-ethyldithio-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (**123**) (5.0 g, 12.0 mmol) in dry CH_2Cl_2 (10 mL) were added levulinic acid (2.08 g, 18 mmol, 1.5 equiv), EDCI (3 g), and an a catalytic amount of 4-dimethylaminopyridine (DMAP). The reaction was stirred at r. t. for 2 h, and then it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography to give compound **124** as a white amorphous solid (4.93 g, 9.6 mmol, 80%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.56; mp 222–223 °C; $[\alpha]_D$ –130.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, 2 H, ArH), 6.86 (d, 2 H, ArH), 6.00 (d, 1 H, NH), 5.44 (s, 1 H, $CH_3OPhC\mathbf{H}$), 5.37 (t, 1 H, H-

3), 4.73 (d, 1 H, H-1, $J_{H1, H2}$ = 10.2 Hz), 4.26 (dd, 1 H, H-6), 4.18 (t, 1 H, H-2), 3.77 (s, 3 H, CH_3O), 3.68 (m, 2 H, H-4, H-6), 3.56 (m, 1 H, H-5), 2.74 (q, 2 H, $SC\mathbf{H}_2CH_3$), 2.62 (m, 2 H, $COC\mathbf{H}_2$), 2.52 (m, 2 H, $COC\mathbf{H}_2$), 2.14 (s, 3 H, CH_3CO), 1.96 (s, 3 H, CH_3CO), 1.28 (t, 3 H, $SCH_2C\mathbf{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.51, 172.91, 170.58, 160.02, 140.48, 129.32, 127.47, 127.21, 113.51, 101.29, 89.65, 78.48, 72.86, 70.47, 68.39, 55.22, 52.75, 37.89, 34.04, 29.68, 28.05, 23.20, 14.32; ESIMS (positive-ion mode): *m/z* 514.0 $[M + H]^+$, 536.0 $[M + Na]^+$, 551.9 $[M + K]^+$. Anal. Calcd for $C_{23}H_{31}NO_8S_2$ (513.15): C, 53.78; H, 6.08; N, 2.73. Found: C, 53.83; H, 6.03; N, 2.69.

2-Acetamido-4,6-di-*O*-acetyl-1,2-dideoxy-1-ethyldithio-3-*O*-levulinoyl-β-D-glucopyranose (126). To a solution of compound **124** (1.5 g, 2.9 mmol) in MeOH (30 mL) and CH_2Cl_2 (6 mL) was added two drops of tetrafloroboric acid (HBF_4). The reaction was stirred at r. t. for 2 h. When TLC showed complete consumption of the starting material and formation of a new spot, the reaction was quenched with triethylamine (TEA) and evaporated to dryness. The resulting diol was redissolved in dry pyridine (5.0 mL, 61.8 mmol) and treated with acetic anhydride (4.0 mL, 42.4 mmol) at r. t. for 10 h, after which time the reaction was quenched with water and diluted with CH_2Cl_2. The solution was washed with a satd $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (10:1 CH_2Cl_2–MeOH) to afford compound **126** as a white amorphous solid. (1.17 g, 2.44 mmol, 84%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.61; mp 155–156 °C; $[\alpha]_D$ –80.6° (*c* 1.0, $CHCl_3$);

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.85 (d, 1 H, NH), 5.33 (t, 1 H, H-3), 5.06 (t, 1 H, H-4), 4.81 (d, 1 H, H-1, $J_{H1, H2}$ = 9.9 Hz), 4.13 (m, 2 H, H-2, H-6), 3.73 (d, 1 H, H-6), 3.19 (m, 1 H, H-5), 2.76 (m, 4 H, $COCH_2$, SCH_2CH_3), 2.46 (m, 2 H, $COCH_2$), 2.14 (s, 3 H, CH_3CO), 2.04 (s, 6 H, CH_3CO), 1.91 (s, 3 H, CH_3CO), 1.28 (t, 3 H, SCH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.68, 172.47, 170.63, 170.55, 169.65, 88.75, 75.80, 73.27, 67.94, 62.18, 52.87, 37.76, 33.85, 29.60, 28.00, 23.26, 20.71, 14.24; ESIMS (positive-ion mode): *m/z* 502.0 $[M + Na]^+$, 517.9 $[M + K]^+$. Anal. Calcd for $C_{19}H_{29}NO_9S_2$ (479.13): C, 47.59; H, 6.10; N, 2.92. Found: C, 47.64; H, 5.99; N, 2.89.

2-Acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-1-thio-β-D-glucopyranose (65). To a solution of compound **126** (200 mg, 0.42 mmol) in THF (4 mL), MeOH (0.6 mL), and triethylamine (TEA) (0.36 mL) was added DTT (50 mg, 0.32 mmol, 0.75 equiv). The reaction was stirred at r. t. for about 1 h, after which time the solvent was evaporated, and the residue was submitted to coarse silica gel column chromatography (65:1 CH_2Cl_2–MeOH) to afford thiol **65** as a white amorphous solid. (140 mg, 0.33 mmol, 80%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.48; mp 150–151 °C; $[\alpha]_D$ –8.0° (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.14 (d, 1 H, NH), 5.15 (t, 1 H, H-3), 5.07 (t, 1 H, H-4), 4.67 (t, 1 H, H-1, $J_{H1, H2}$ = 9.3 Hz), 4.21 (dd, 1 H, H-6), 4.08 (dd, 1 H, H-6), 3.98 (t, 1 H, H-2), 3.68 (m, 1 H, H-5), 2.72 (q, 2 H, $COCH_2$), 2.51 (d, 1 H, SH), 2.45 (m, 2 H, $COCH_2$), 2.14 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 1.96 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.65, 172.71, 171.01, 170.79, 169.51, 79.79, 75.96, 73.33, 67.80, 62.09, 56.84, 37.66, 29.56, 27.98, 23.22, 20.76, 20.62; ESIMS

(positive-ion mode): *m/z* 442.0 $[M + Na]^+$, 458.0 $[M + K]^+$. Anal. Calcd for $C_{17}H_{25}NO_9S$ (419.13): C, 48.68; H, 6.01; N, 3.34. Found: C, 48.82; H, 5.93; N, 3.22.

Allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (64). To a solution of 2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-1-thio-*β*-D-glucopyranose (**65**) (1.3 g, 2.87 mmol) and Cs_2CO_3 (1.44 g, 4.42 mmol) in dry DMF (5.0 mL) was added a solution of triflate **58** (3.3 g, 5.94 mmol) in dry DMF (5.0 mL) at 0 °C. The reaction was stirred at 0 °C for 2 h, after which time it was quenched with water and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (70:1 CH_2Cl_2–MeOH) to afford compound **64** as a colorless foam (2.1 g, 2.54 mmol, 88%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.81; mp 75–76 °C; $[\alpha]_D$ –54.0° (*c* 0.25, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.27 (d, 2 H, ArH), 6.90 (d, 2 H, ArH), 5.84 (m, 1 H, C**H**=CH_2), 5.56 (d, 1 H, NH), 5.25 (dd, 1 H, CH=C**H**$_2$), 5.18 (dd, 1 H, CH=C**H**$_2$), 5.11 (dd, 1 H, H-3^I), 5.02 (t, 1 H, H-2^I), 5.00 (t, 1 H, H-3^{II}), 4.96 (t, 1 H, H-4^{II}), 4.72 (d, 1 H, H-1^{II}, $J_{H1,H2}$ = 10.8 Hz), 4.58 (d, 1 H, $ArCH_2O$), 4.46 (d, 1 H, $ArCH_2O$), 4.44 (d, 1 H, H-1^I, $J_{H1,H2}$ = 7.8 Hz), 4.33 (m, 1 H, $OCH_2CH=CH_2$), 4.06 (m, 4 H, H-2^{II}, H-6^{II}, $OCH_2CH=CH_2$), 3.94 (dd, 1 H, H-6^I), 3.83 (m, 1 H, H-6^I), 3.82 (s, 3 H, OCH_3), 3.69 (dd, 1 H, H-5^I), 3.55 (dt, 1 H, H-5^{II}), 3.04 (t, 1 H, H-4^I), 2.71 (t, 2 H, $COCH_2$), 2.46 (t, 2 H, $COCH_2$), 2.15 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 1.89 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ

206.55, 172.49, 171.59, 170.60, 170.12, 169.89, 169.58, 159.49, 133.78, 130.32, 129.80, 117.41, 114.05, 99.86, 82.59, 75.91, 75.78, 74.41, 73.55, 72.65, 70.91, 69.78, 68.89, 68.25, 62.80, 55.50, 52.62, 46.12, 37.90, 29.82, 28.23, 23.27, 21.15, 21.00, 20.89, 20.86; ESIMS (positive-ion mode): *m/z* 848.2 $[M + Na]^+$, 864.2 $[M + K]^+$. Anal. Calcd for $C_{38}H_{51}NO_{17}S$ (825.29): C, 55.26; H, 6.22; N, 1.70. Found: C, 54.89; H, 6.10; N, 1.57.

S-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α,β-D-glucopyranose (127). (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (30 mg) was suspended in dry tetrahydrofuran (THF) (5.0 mL) and treated with H_2 at r. t. for 15 min until the solids had completely dissolved and the red color had completely changed to a pale tan color. Then the solution was evacuated, purged with N_2, and added to a 50-mL flask containing **64** (500 mg, 0.61 mmol) under N_2. The reaction was stirred at r. t. for 3 days, after which time it was cooled down to 0 °C, and a solution of $NaHCO_3$ (207 mg, 2.46 mmol) in water (5 mL) and I_2 (500 g, 1.95 mmol) was added. The reaction was stirred at 0 °C for another 20 min, then it was diluted with water and CH_2Cl_2. Solid sodium thiosulfate was added until the iodine color completely disappeared. The mixture was extracted with CH_2Cl_2, and the combined organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (60:1 CH_2Cl_2–MeOH) to afford compound **127**, with an α, β anomeric ratio of 1:2, as a white amorphous solid (440 mg, 0.56 mmol, 92%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.50; ^1H NMR (600 MHz, $CDCl_3$): δ 7.27 (d, 2 H, β-ArH), 7.25 (d, 1

H, α-ArH), 6.91 (d, 2 H, β-ArH), 6.89 (d, 1 H, α-ArH), 5.73 (d, 0.5 H, α-NH), 5.55 (d, 1 H, β-NH), 5.51 (dd, 0.5 H, α-H-3^{I}), 5.48 (t, 0.5 H, α-H-1^{I}, $J_{H1, H2}$ = 3.0 Hz, $J_{H1, OH}$ = 3.6 Hz), 5.15 (dd, 1H, β-H-3^{I}), 5.05 (t, 1 H, α-H-3^{II}), 5.04 (t, 1 H, β-H-3^{II}), 5.02 (t, 0.5 H, α-H-4^{II}), 4.97 (t, 1 H, β-H-4^{II}), 4.92 (dd, 0.5 H, α-H-2^{I}), 4.84 (dd, 1 H, β-H-2^{I}), 4.80 (d, 0.5 H, α-H-1^{II}, $J_{H1, H2}$ = 10.8 Hz), 4.74 (d, 1 H, β-H-1^{II}, $J_{H1, H2}$ =10.2 Hz), 4.59 (dd, 1 H, β-H-1^{I}, $J_{H1, H2}$ = 8.4 Hz, $J_{H1, OH}$ = 8.4 Hz,), 4.57 (d, 1 H, β-$ArCH_2O$), 4.55 (d, 0.5 H, α-$ArCH_2O$), 4.46 (d, 1 H, β-$ArCH_2O$), 4.45 (d, 0.5 H, α-$ArCH_2O$), 4.38 (m, 0.5 H, α-H-5^{I}), 4.16–4.04 (m, 3 H, β-H-2^{II}, α-H-2^{II}, β-H-6^{II}, α-H-6^{II}), 3.97 (m, 1.5 H, β-H-6^{I}, α-H-6^{I}), 3.82 (s, 4.5 H, α-CH_3O, β-CH_3O), 3.81–3.71 (m, 2.5 H, β-H-6^{I}, α-H-6^{I}, β-H-5^{I}), 3.60 (m, 1 H, β-H-5^{II}), 3.57 (m, 0.5 H, α-H-5^{II}), 3.08 (t, 1 H, β-H-4^{I}), 3.03 (t, 0.5 H, α-H-4^{I}), 2.71 (t, 3 H, α-$COCH_2$, β-$COCH_2$), 2.47 (m, 3 H, α-$COCH_2$, β-$COCH_2$), 2.15 (s, 3 H, β-CH_3CO), 2.10 (s, 3 H, β-CH_3CO), 2.09 (s, 1.5 H, α-CH_3CO), 2.08 (s, 3 H, α-CH_3CO), 2.07 (s, 7.5 H, β-CH_3CO, α-CH_3CO), 2.06 (s, 1.5 H, α-CH_3CO), 2.03 (s, 3 H, β-CH_3CO), 1.91 (s, 1.5 H, α-CH_3CO), 1.89 (s, 3 H, β-CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.34, 172.21, 172.14, 171.34, 171.19, 170.70, 170.63, 170.43, 170.01, 169.63, 159.28, 159.19, 129.87, 129.71, 129.56, 113.81, 113.74, 95.36, 90.08, 82.11, 81.91, 75.51, 75.40, 74.38, 74.04, 73.34, 73.29, 72.41, 70.03, 69.81, 68.73, 68.62, 67.98, 67.90, 67.37, 62.39, 62.31, 55.23, 52.30, 52.11, 45.72, 37.60, 29.52, 27.92, 22.93, 20.97, 20.84, 20.77, 20.67, 20.60; ESIMS (positive-ion mode): *m/z* 808.0 $[M + Na]^+$, 824.0 $[M + K]^+$. Anal. Calcd for $C_{35}H_{47}NO_{17}S$ (785.26): C, 53.50; H, 6.03; N, 1.78. Found: C, 53.23; H, 5.96; N, 1.80.

***S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α, β-D-glucopyranosyl trichloroacetimidate (66).** To a mixture of compound **127** (300 mg, 0.38 mmol) and trichloroacetonitrile (0.42 mL, 4.2 mmol) in dry CH_2Cl_2 (2 mL) was added 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) (2 drops). The reaction was stirred at r. t. for 40 min, and then it was concentrated and submitted to coarse silica gel column chromatography (1:5 hexanes–EtOAc) to afford trichloroacetimidate **66**, with an α, β anomeric ratio of 8:1, as an unstable colorless foam (289 mg, 82%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.69 (α anomer); $[\alpha]_D$ +17.6° (*c* 0.5, $CHCl_3$, α anomer); mp 79–80 °C; ^{1}H NMR (600 MHz, $CDCl_3$, α anomer): δ 8.62 (s, 1 H, C=NH), 7.26 (d, 2 H, ArH), 6.90 (d, 2 H, ArH), 6.60 (d, 1 H, H-1^I, $J_{H1, H2}$ = 3.6 Hz), 5.66 (d, 1 H, NH), 5.54 (dd, 1 H, H-3^I), 5.10 (dd, 1 H, H-2^I), 5.03 (t, 1 H, H-3^{II}), 4.99 (t, 1 H, H-4^{II}), 4.72 (d, 1 H, H-1^{II}, $J_{H1, H2}$ = 10.2 Hz), 4.54 (d, 1 H, $ArCH_2O$), 4.46 (d, 1 H, $ArCH_2O$), 4.30 (m, 1 H, H-5^I), 4.14 (t, 1 H, H-2^{II}), 4.10 (m, 1 H, H-6^I), 4.04 (m, 2 H, H-6^{II}), 3.81 (s, 3 H, OCH_3), 3.67 (dd, 1 H, H-6^I), 3.50 (m, 1 H, H-5^{II}), 3.24 (t, 1 H, H-4^I), 2.71 (t, 2 H, $COCH_2$), 2.47 (t, 2 H, $COCH_2$), 2.15 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.98 (s, 3 H, CH_3CO), 1.91 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$, α anomer): δ 206.48, 172.51, 171.49, 170.53, 170.11, 170.04, 169.82, 161.01, 159.55, 130.11, 129.84, 114.05, 94.34, 82.25, 75.74, 74.55, 73.75, 73.68, 71.34, 68.29, 68.12, 67.22, 62.59, 55.50, 52.25, 45.26, 37.88, 29.81, 28.25, 23.25, 21.26, 20.88, 20.75; ESIMS (positive-ion mode): *m/z* 951.0 $[M + Na]^+$, 967.0 $[M + K]^+$. Anal. Calcd for $C_{37}H_{47}Cl_3N_2O_{17}S$ (928.17): C, 47.77; H, 5.09; N, 3.01. Found: C, 47.99; H, 4.96; N, 3.04.

Allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (67). To a solution of compound **64** (200 mg, 0.28 mmol) in acetic acid (0.5 mL) and pyridine (0.8 mL) was added hydrazine hydrate (0.1 mL) at 0 °C. The reaction was stirred for 10 min, after which time it was diluted with CH_2Cl_2, washed with satd $NaHCO_3$, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (50:1 CH_2Cl_2–MeOH) to afford compound **67** as a colorless foam (181 mg, 0.25 mmol, 89%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.52; mp 86–87 °C; $[\alpha]_D$ –80.4° (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25 (d, 2 H, ArH), 6.88 (d, 2 H, ArH), 6.33 (d, 1 H, NH), 5.84 (m, 1 H, C**H**=CH_2), 5.22 (dd, 1 H, CH=C**H**$_2$), 5.18 (dd, 1 H, CH=C**H**$_2$), 5.18 (t, 1 H, H-3^I), 5.05 (t, 1 H, H-2^I), 4.87 (m, 1 H, H-4^{II}), 4.65 (d, 1 H, H-1^{II}, $J_{H1,\,H2}$ = 9.0 Hz), 4.57 (d, 1 H, $ArCH_2O$), 4.47 (d, 1 H, $ArCH_2O$), 4.44 (d, 1 H, H-1^I, $J_{H1,\,H2}$ = 7.8 Hz), 4.34 (dd, 1 H, O**C**H$_2$CH=CH_2), 4.12 (d, 1 H, H-6^{II}), 4.07 (dd, 1 H, O**C**H$_2$CH=CH_2), 4.05 (m, 1 H, H-6^{II}), 4.01 (m, 1 H, H-6^I), 3.84 (m, 1 H, H-6^I), 3.82 (s, 3 H, OCH_3), 3.81 (m, 1 H, H-2^I), 3.74 (dd, 1 H, H-5^I), 3.62 (t, 1 H, H-3^{II}), 3.54 (m, 1 H, H-5^{II}), 3.07 (t, 1 H, H-4^I), 2.13 (s, 3 H, CH_3CO), 2.11 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.79, 172.67, 170.57, 170.45, 169.48, 159.47, 133.72, 130.29, 129.70, 117.43, 113.97, 99.83, 81.14, 77.00, 75.72, 75.68, 73.59, 72.45, 71.40, 71.25, 69.76, 68.75, 63.15, 55.97, 55.51, 46.43, 22.98, 21.38, 21.12, 20.98, 20.87; ESIMS (positive-ion mode): *m/z* 728.1 $[M + H]^+$, 750.1 $[M + Na]^+$, 766.0 [M +

K]$^+$. Anal. Calcd for $C_{33}H_{45}NO_{15}S$ (727.25): C, 54.46; H, 6.23; N, 1.92. Found: C, 54.27; H, 6.19; N, 1.83.

Allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (128). To a solution of acceptor **67** (300 mg, 0.41 mmol) in 1,2-dichloroethane ($C_2H_4Cl_2$) was added TMSOTf (0.01 M in $C_2H_4Cl_2$, 0.1 mL) at –15 °C under N_2. The mixture was stirred for 10 min, and then a solution of trichloroacetimidate **66** (590 mg, 0.63 mmol, 1.53 equiv) in 1,2-dichloroethane ($C_2H_4Cl_2$) was added. The reaction was stirred at –15 °C under N_2 for another 2 h, after which time it was quenched with triethylamine (TEA), filtered, and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (50:1 CH_2Cl_2–MeOH) to afford compound **128** as a white amorphous solid (428 mg, 0.29 mmol, 69%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.50; $[\alpha]_D$ +10.4° (*c* 0.5, $CHCl_3$); mp 122–123 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 (d, 2H, ArH), 7.25 (d, 2H, ArH), 6.90 (d, 2 H, ArH), 6.89 (d, 2 H, ArH), 5.85 (m, 1 H, C**H**=CH_2), 5.75 (d, 1 H, NH^{II}), 5.61 (d, 1 H, NH^{IV}), 5.25 (m, 1 H, CH=C**H**$_2$), 5.18 (d, 1 H, CH=C**H**$_2$), 5.10 (t, 1 H, H-3^{I}), 5.08 (t, 1 H, H-3^{IV}), 5.05 (t, 2 H, H-3^{III}, H-4^{IV}), 4.98 (t, 1 H, H-2^{I}), 4.80 (t, 1 H, H-4^{II}), 4.77 (d, 1 H, H-1^{IV}, $J_{H1,H2}$ = 10.8 Hz), 4.74 (t, 1 H, H-2^{III}), 4.65 (d, 1 H, H-1^{II}, $J_{H1,H2}$ = 10.2 Hz), 4.58 (d, 1 H, H-1^{III}, $J_{H1,H2}$ = 7.8 Hz), 4.55 (d, 1 H, $ArCH_2O$), 4.50 (d, 1 H, $ArCH_2O$), 4.45 (d, 1 H, $ArCH_2O$), 4.44 (d, 1 H, H-1^{I}, $J_{H1,H2}$ = 7.8 Hz), 4.42 (d, 1 H,

$ArCH_2O$), 4.33 (dd, 1 H, $OCH_2CH=CH_2$), 4.20 (dd, 1 H, H-6^{IV}), 4.12 (m, 2 H, H-6^{IV}, H-6^{II}), 4.04 (m, 3 H, $OCH_2CH=CH_2$, H-6^{II}, H-2^{IV}), 3.94 (m, 3 H, H-6^{I}, H-6^{III}, H-2^{II}), 3.86 (dd, H-6^{III}), 3.82 (s, 6 H, OCH_3), 3.81 (m, 2 H, H-6^{I}, H-3^{II}), 3.69 (m, 2 H, H-5^{III}, H-5^{I}), 3.59 (m, 1 H, H-5^{II}), 3.55 (m, 1 H, H-5^{IV}), 3.05 (t, 1 H, H-4^{I}), 3.01 (t, 1 H, H-4^{III}), 2.72 (t, 2 H, $COCH_2$), 2.46 (t, 2 H, $COCH_2$), 2.15 (s, 3 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 1.95 (s, 6 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.21, 172.12, 171.39, 171.15, 170.60, 170.29, 169.92, 169.53, 169.49, 169.45, 169.16, 159.23, 158.97, 133.43, 130.09, 129.64, 129.46, 129.38, 117.00, 113.76, 113.61, 100.05, 99.46, 81.93, 81.74, 78.71, 75.54, 75.29, 75.10, 73.78, 73.10, 72.98, 72.52, 72.44, 70.62, 69.39, 68.85, 68.55, 68.45, 67.91, 62.83, 61.95, 55.14, 53.42, 52.62, 45.45, 45.22, 37.54, 29.43, 27.84, 23.10, 22.90, 20.83, 20.68, 20.63, 20.60, 20.52; ESIMS (positive-ion mode): *m/z* 1495.3 $[M + H]^+$, 1512.3 $[M + NH_4]^+$, 1517.3 $[M + Na]^+$, 1533.3 $[M + K]^+$. Anal. Calcd for $C_{68}H_{90}N_2O_{31}S_2$ (1495.57): C, 54.61; H, 6.07; N, 1.87. Found: C, 54.15; H, 6.24; N, 1.83.

Allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (129). To a solution of tetrasaccharide **128** (150 mg, 0.10 mmol) in acetic acid (0.3 mL) and pyridine (0.4 mL) was added hydrazine hydrate (0.2 mL) at 0 °C. The reaction was stirred for 10 min, after which time it was

diluted with CH_2Cl_2, washed with a satd $NaHCO_3$ solution, and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (50:1 CH_2Cl_2–MeOH) to afford compound **129** as a colorless foam (123 mg, 0.088 mmol, 88%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.37; mp 197–198 °C; $[\alpha]_D$ –74.8° (*c* 0.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25 (d, 2H, ArH), 7.23 (d, 2H, ArH), 6.89 (d, 2 H, ArH), 6.88 (d, 2 H, ArH), 6.23 (d, 1 H, NH^{IV}), 5.85 (m, 1 H, C**H**=CH_2), 5.78 (d, 1 H, NH^{II}), 5.25 (dd, 1 H, CH=C**H**$_2$), 5.17 (dd, 1 H, CH=C**H**$_2$), 5.14 (dd, 1 H, H-3^I), 5.10 (dd, 1 H, H-3^{III}), 4.99 (t, 1 H, H-2^{III}), 4.94 (t, 1 H, H-4^{IV}), 4.81 (t, 1 H, H-4^{II}), 4.80 (t, 1 H, H-2^I), 4.71 (d, 1 H, H-1^{IV}, $J_{H1, H2}$ = 10.8 Hz), 4.66 (d, 1 H, H-1^{II}, $J_{H1, H2}$ = 10.2 Hz), 4.61 (d, 1 H, H-1^I, $J_{H1, H2}$ = 7.8 Hz), 4.55 (d, 1 H, $ArCH_2O$), 4.49 (d, 1 H, $ArCH_2O$), 4.45 (d, 1 H, $ArCH_2O$), 4.44 (d, 1 H, H-1^{III}, $J_{H1, H2}$ = 8.4 Hz), 4.42 (d, 1 H, $ArCH_2O$), 4.33 (m, 1 H, OC**H**$_2$CH=CH_2), 4.21 (dd, 1 H, H-6^{IV}), 4.12 (m, 2 H, H-6^{IV}, H-6^{II}), 4.07 (m, 1 H, OC**H**$_2$CH=CH_2), 4.05 (m, 1 H, H-6^{II}), 3.96 (m, 3 H, H-6^I, H-6^{III}, H-2^{II}), 3.88 (d, 1 H, H-6^I), 3.82 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.81 (m, 3 H, H-3^{II}, H-2^{IV}, H-6^{III}), 3.73 (m, 1 H, H-5^I), 3.66 (m, 2 H, H-3^{IV}, H-5^{III}), 3.63 (m, 1 H, H-5^{II}), 3.58 (m, 1 H, H-5^{IV}), 3.05 (t, 1 H, H-4^{III}), 3.03 (t, 1 H, H-4^I), 2.11 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 2.014 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 1.94 (s, 6 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.28, 172.11, 171.63, 170.82, 170.37, 170.14, 169.67, 169.56, 169.54, 169.25, 159.29, 159.05, 133.49, 130.14, 129.65, 129.46, 129.39, 117.07, 113.76, 113.67, 99.87, 99.50, 81.66, 80.76, 78.50, 75.99, 75.66, 75.59, 75.11, 75.01, 73.19, 73.13, 72.56, 72.40, 71.10,

71.02, 70.67, 69.47, 68.91, 68.66, 68.54, 62.94, 62.51, 55.66, 55.22, 53.40, 45.68, 45.56, 23.14, 22.77, 20.95, 20.90, 20.79, 20.74, 20.65, 20.58; ESIMS (positive-ion mode): *m/z* 1397.4 $[M + H]^+$, 1414.4 $[M + NH_4]^+$, 1419.3 $[M + Na]^+$, 1435.3 $[M + K]^+$. Anal. Calcd for $C_{63}H_{84}N_2O_{29}S_2$ (1396.46): C, 54.15; H, 6.06; N, 2.00. Found: C, 53.86; H, 6.20; N, 1.93.

Allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (130). To a solution of acceptor **129** (68 mg, 0.048 mmol) in $C_2H_4Cl_2$ was added TMSOTf (0.01 M in $C_2H_4Cl_2$, 0.1 mL) at –15 °C under N_2. The mixture was stirred for 10 min, and then a solution of trichloroacetimidate **66** (66.8 mg, 0.072 mmol, 1.5 equiv) in $C_2H_4Cl_2$ was added. The reaction was stirred at –15 °C under N_2 for 1 h, and then another 1.5 equiv of trichloroacetimiadte **66** (66.8 mg, 0.072 mmol) was added along with another catalytic amount of TMSOTf (0.01 M in $C_2H_4Cl_2$, 0.1 mL). The reaction was then stirred at –15 °C under N_2 for another 2 h, after which time it was quenched with triethylamine (TEA) and evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (50:1 CH_2Cl_2–MeOH) to afford hexasaccharide **130** as a white amorphous solid (48.5 mg, 0.022 mmol, 46%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.38; $[\alpha]_D$ –38.4° (*c* 0.5, CH_2Cl_2); mp 133–134 °C; ^{1}H NMR (600

MHz, $CDCl_3$): δ 7.25 (d, 4 H, ArH), 7.23 (d, 2 H, ArH), 6.91 (d, 2 H, ArH), 6.89 (d, 2 H, ArH), 6.88 (d, 2 H, ArH), 5.90 (d, 1 H, NH^{IV}), 5.84 (m, 1 H, C**H**=CH_2), 5.74 (d, 1 H, NH^{II}), 5.57 (d, 1 H, NH^{VI}), 5.25 (dd, 1 H, CH=C**H**$_2$), 5.18 (dd, 1 H, CH=C**H**$_2$), 5.10 (m, 4 H, H-3^{I}, H-3^{III}, H-3^{V}, H-3^{VI}), 5.05 (m, 2 H, H-2^{V}, H-4^{VI}), 4.99 (t, 1 H, H-2^{I}), 4.87 (m, 1 H, H-4^{IV}), 4.80 (t, 1 H, H-4^{II}), 4.79 (d, 1 H, H-1^{IV}, $J_{H1, H2}$ = 9.0 Hz), 4.78 (d, 1 H, H-1^{VI}, $J_{H1, H2}$ = 9.6 Hz), 4.77 (t, 1 H, H-2^{III}), 4.69 (d, 1 H, H-1^{II}, $J_{H1, H2}$ = 8.4 Hz), 4.64 (d, 1 H, H-1^{V}, $J_{H1, H2}$ = 8.4 Hz), 4.62 (d, 1 H, H-1^{III}, $J_{H1, H2}$ = 7.2 Hz), 4.54 (d, 1 H, $ArCH_2O$), 4.50 (d, 1 H, $ArCH_2O$), 4.46 (d, 1 H, $ArCH_2O$), 4.45 (d, 1 H, $ArCH_2O$), 4.43 (d, 1 H, H-1^{I}, $J_{H1, H2}$ = 7.8 Hz), 4.42 (d, 1 H, $ArCH_2O$), 4.40 (d, 1 H, $ArCH_2O$), 4.33 (m, 1 H, O**C**H_2CH=CH_2), 4.24 (m, 1 H, H-6^{I}), 4.21 (m, 1 H, H-6^{VI}), 4.11 (dd, 2 H, H-6^{VI}, H-6^{II}), 4.04 (m, 3 H, O**C**H_2CH=CH_2, H-2^{VI}, H-6^{II}), 3.94 (m, 5 H, H-2^{IV}, H-6^{III}, H-6^{V}, H-6^{IV}, H-2^{II}), 3.84 (m, 5 H, H-6^{V}, H-6^{IV}, H-6^{III}, H-3^{II}, H-3^{IV}), 3.83 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.70 (m, 3 H, H-5^{I}, H-5^{III}, H-5^{V}), 3.66 (m, 1 H, H-5^{IV}), 3.59 (m, 1 H, H-5^{II}), 3.56 (m, 1 H, H-5^{VI}), 3.04 (t, 1 H, H-4^{I}), 3.03 (t, 1 H, H-4^{III}), 3.00 (t, 1 H, H-4^{V}), 2.72 (t, 2 H, CO**C**H_2), 2.46 (t, 2 H, CO**C**H_2), 2.16 (s, 3 H, CH_3CO), 2.09 (s, 6 H, CH_3CO), 2.07 (s, 6 H, CH_3CO), 2.06 (s, 6 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.95 (s, 3 H, CH_3CO), 1.94 (s, 3 H, CH_3CO), 1.90 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.28, 172.24, 171.57, 171.46, 171.26, 171.06, 170.74, 170.39, 170.00, 169.71, 169.59, 169.54, 169.26, 159.34, 159.19, 159.10, 133.54, 130.20, 129.83, 129.73, 129.50, 117.09, 113.86, 113.79, 113.70, 99.91, 99.57, 82.04, 81.81, 81.24, 78.70, 78.53, 77.21, 75.66, 75.41, 75.22, 73.93, 73.20, 73.13, 72.60, 70.65, 70.49, 69.48, 68.89, 68.66, 68.00, 62.97,

62.54, 62.03, 55.25, 53.42, 52.69, 45.59, 45.34, 45.24, 37.65, 29.65, 29.53, 27.97, 25.45, 23.22, 23.14, 23.01, 20.85, 20.63; ESIMS (positive-ion mode): *m/z* 2164.7 $[M + H]^+$, 2186.6 $[M + Na]^+$, 2202.6 $[M + K]^+$; MALDIMS (positive-ion mode): *m/z* 2186.4339 $[M + Na]^+$. Anal. Calcd for $C_{98}H_{129}N_3O_{45}S_3$ (2163.71): C, 54.36; H, 6.01; N, 1.94. Found: C, 54.01; H, 6.17; N, 1.92.

Allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranoside (131). To a solution of hexasaccharide **130** (43 mg, 0.02 mmol) in CH_2Cl_2 (5 mL) and H_2O (0.3 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (27 mg, 0.12 mmol, 6 equiv). After stirring for 1.5 h, the mixture was poured into a satd $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic phase was dried with anhyd Na_2SO_4 and then evaporated to dryness. The residue was submitted to coarse silica gel column chromatography (20:1 CH_2Cl_2–MeOH) to afford compound **131** as a white amorphous solid (30 mg, 0.017 mmol, 83%). TLC (10:1 $CHCl_3$–MeOH): R_f 0.32; $[\alpha]_D$ –54.2° (*c* 0.5, CH_2Cl_2); mp 255–256 °C; ^{1}H NMR (600 MHz, 5:1 $CDCl_3$–CD_3OD): δ 5.84 (m, 1 H, C**H**=CH_2), 5.26 (d, 1 H, CH=C**H**$_2$), 5.20 (d, 1 H, CH=C**H**$_2$), 5.17 (t, 1 H, H-3^{VI}), 5.06 (m, 4 H, H-3^{I}, H-3^{III}, H-3^{V}, H-4^{VI}), 4.91 (m, 3 H, H-2^{I}, H-4^{IV}, H-4^{II}), 4.82 (d, 1 H, H-1^{VI}, $J_{H1, H2}$ = 10.2 Hz), 4.72 (m, 2 H, H-2^{III}, H-2^{V}), 4.63 (m, 4 H, H-1^{II}, H-1^{IV}, H-1^{III}, H-1^{V}, $J_{H1, H2}$

= 7.2 Hz, 7.8 Hz, 10.8 Hz), 4.51 (d, 1 H, H-1^{I}, $J_{H1, H2}$ = 7.8 Hz), 4.33 (dd, 1 H, $OCH_2CH=CH_2$), 4.22 (m, 2 H, H-6^{VI}), 4.15 (m, 4 H, H-6^{II}, H-6^{IV}), 4.10 (dd, 1 H, $OCH_2CH=CH_2$), 3.96 (m, 8 H, H-2^{II}, H-2^{IV}, H-6^{III}, H-6^{I}, H-6^{V}, H-3^{II}, H-3^{IV}), 3.83 (m, 2 H, H-6^{V}, H-6^{III}), 3.70 (m, 3 H, H-5^{II}, H-5^{IV}, H-5^{VI}), 3.54 (m, 3 H, H-5^{I}, H-5^{III}, H-5^{V}), 3.00 (t, 1 H, H-4^{I}), 2.87 (dt, 2 H, H-4^{III}, H-4^{V}), 2.74 (t, 2 H, $COCH_2$), 2.47 (t, 2 H, $COCH_2$), 2.17 (s, 3 H, CH_3CO), 2.12 (s, 12 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 22.07 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.03 (s, 6 H, CH_3CO), 2.028 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.98 (s, 3 H, CH_3CO), 1.92 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, 5:1 $CDCl_3$–CD_3OD): δ 207.02, 172.17, 171.18, 170.97, 170.84, 170.10, 169.95, 169.77, 133.12, 117.16, 99.31, 99.17, 83.95, 83.34, 78.56, 75.30, 75.10, 74.95, 73.48, 72.57, 71.37, 71.16, 70.92, 69.72, 68.32, 67.84, 62.54, 62.04, 61.71, 61.27, 60.97, 53.46, 52.69, 45.92, 45.74, 37.38, 29.43, 29.22, 27.67, 22.56, 22.35, 20.39, 20.24; MALDIMS (positive-ion mode): 1825.9617 $[M + Na]^+$, 1841.9717 $[M + K]^+$. Anal. Calcd for $C_{74}H_{105}N_3O_{42}S_3$ (1804.82): C, 49.25; H, 5.86; N, 2.33. Found: C, 48.91; H, 6.05; N, 2.29.

Allyl *S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-(4-thio-β-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-(4-thio-β-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-4-thio-β-D-glucopyranosiduronic acid (133). To a solution of compound **131** (40 mg, 0.022 mmol) in dry DMF (2 mL) was added pyridinium dichromate (PDC) (249 mg, 0.066 mmol, 30 equiv). The reaction was allowed to stir at r.

t. for 2 days, after which time it was evaporated to dryness and the residue was submitted to coarse silica gel column chromatography (10:1:1 CH_2Cl_2–MeOH–AcOH) to afford compound **132** as a white amorphous solid (28 mg, 0.015 mmol, 69%). The resulting solid was redissolved in 1:2 THF and water (3 mL) and treated with lithium hydroxide monohydride (16.5 mg, 0.39 mmol, 26 equiv) at r. t. for 10 h. After which time the reaction mixture was neutralized with Dowex–50 × 2 (H^+ form), filtered, and evaporated to dryness. The residue was purified by Sephadex G-10 size-exclusion column chromatography (20 cm) using water as solvent to give compound **133** as a white amorphous solid (15 mg, 0.012 mmol, 80%). ^{1}H NMR (600 MHz, D_2O): δ 5.92 (m, 1 H, C**H**=CH_2), 5.35 (d, 1 H, CH=C**H**$_2$), 5.25 (d, 1 H, CH=C**H**$_2$), 4.59 (m, 3 H, H-1^{II}, H-1^{IV}, H-1^{VI}), 4.49 (m, 3 H, H-1^{I}, H-1^{III}, H-1^{V}), 4.33 (d, 1 H, OC**H**$_2$CH=CH_2), 4.18 (m, 1 H, OC**H**$_2$CH=CH_2), 4.01 (d, 1 H, H-3^{I}), 3.96 (d, 2 H, H-3^{III}, H-3^{V}), 3.89 (d, 3 H, H-6^{II}, H-6^{IV}, H-6^{VI}), 3.85 (m, 1 H, H-2^{VI}), 3.71 (m, 8 H, H-6^{II}, H-6^{IV}, H-6^{VI}, H-2^{II}, H-2^{IV}, H-3^{II}, H-3^{IV}, H-3^{VI}), 3.52 (t, 3 H, H-4^{II}, H-4^{IV}, H-4^{VI}), 3.44 (m, 6 H, H-5^{I}, H-5^{II}, H-5^{III}, H-5^{IV}, H-5^{V}, H-5^{VI}) 3.34 (m, 3 H, H-2^{I}, H-2^{III}, H-2^{V}), 2.97 (t, 3 H, H-4^{I}, H-4^{III}, H-4^{V}), 2.01 (s, 3 H, CH_3CO), 1.98 (s, 6 H, CH_3CO); MALDIMS (negative-ion mode): 1242.3100 $[M - H]^-$, 1264.2767 $[M - 2H + Na]^-$, 1280.2525 $[M - 2H + K]^-$, 1286.2227 $[M - 3H + 2Na]^-$, 1297.2186 $[M - 3H + NH_4 + K]^-$; MALDIMS (positive-ion mode): 1266.4201 $[M + Na]^+$, 1288.4309 $[M - H + 2Na]^+$.

REFERENCES

1. Stryer, L. *Biochemistry, 4th ed.*; W. H. Freeman: New York, **1995**, pp 474-475.

2. Akima, K.; Ito, H.; Iwata, Y.; Matsuo, K.; Watari, N.; Yanagi, M.; Hagi, H.; Oshima, K.; Yagita, A. *J. Drug Targeting*, **1996**, *4*, 1-8.

3. Spruss, T.; Bernhardt, G. *Contrib. Oncol.* **1996**, *51*, 145-150.

4. Pouyani, T.; Harbison, G. S.; Prestwich, G. D. *J. Am. Chem. Soc.* **1994**, *116*, 7515-7522.

5. Sy, M. S.; Liu, D.; Schiavone, R.; Ma, J.; Mori, H.; Guo, Y. *Curr. Top. Microbiol. Immunol.* **1996**, *213*, 129-153.

6. Entwistle, J.; Hall, C. L.; Turley, E. A. *J. Cell. Biochem.* **1996**, *61*, 569-577.

7. Knudson, W. *Am. J. Pathol.* **1996**, *148*, 1721-1726.

8. Buick, R. N. *In Antineoplastic Agents*, Remers, W. A., Ed.; Wiley: New York, **1984**, p. 3.

9. Fildler, I.; Hart, I. *Science*, **1982**, *217*, 998-1003.

10. Frixen, U. H.; Behrens, J.; Sachs, M.; Eberle, G.; Voss, B.; Warda, A.; Lochner, D.; Birchmeier, W. *J. Cell Biol.* **1991**, *113*, 173-185.

11. Stetler-Stevenson, W.; Aznavoorian, S.; Liotta, L. *Annu. Rev. Cell. Biol.* **1993**, *9*, 541-574.

12. Takeichi, M. *Curr. Opin. Cell Biol.* **1993**, *5*, 806-811.

13. Zetter, B. *Semin. Cancer Biol.* **1993**, *4*, 219-229.

14. Albeld, S. M. *Adhesion Molecules*, Wegner, C. D., Ed.; Academic: New York, **1994**; Chapter 4.

15. Castronovo, V.; Taraboletti, G.; Sobol, M. *J. Biol. Chem.* **1991**, *266*, 20440-20446.

16. Dejana, E.; Martin-Padura, I.; Lauri, D.; Bernasconi, S.; Bani, M.; Garofolo, A.; Giavazzi, R.; Magnani, J.; Mantovani, A.; Menard, S. *Lab. Invest.* **1992**, *66*, 324-330.

17. Sneath, R. J. S.; Mangham, D. C. *Mol. Pahtol.* **1998**, *51*, 191-200.

18. Jackson, D. G.; Buckley, J.; Bell, J. I. *J. Biol. Chem.* **1992**, *267*, 4732-4739.

19. Laurent, T. C.; Fraser, J. R. E. *Functions of the Proteoglycans* (CIBA Foundation Symposium 124); Evered, D., Whelan, J., Eds.; Wiley: Chichester **1986**; pp 9-29.

20. Toole, B. P.; Biswas, C.; Gross, J. *Proc. Natl. Acad. Sci. USA* **1979**, *76*, 6299-6309.

21. Knudson, W.; Biswas, C.; Toole, B. P. *Proc. Natl, Acad. Sci. USA* **1984**, *81*, 6767-6771.

22. Knudson, W.; Biswas, C.; Toole, B. P. *J. Cell. Biochem.* **1989**, *25*, 183-196.

23. Knudson, C. B.; Knudson, W. *Cancer Lett.* **1990**, *52*, 113-122.

24. Nemec, R. E.; Toole, B. P.; Knudson, W. *Biochem. Biophys. Res. Commun.* **1987**, *149*, 249-257.

25. Hofmann, M.; Rudy, R.; Zöller, M.; Tölg, C.; Ponta, H.; Herrlich, P.; Günthert, U. *Cancer Res.* **1991**, *51*, 5292-5297.

26. Birch, M.; Mitchell, S.; Hart, I. *Cancer Res.* **1991**, *51*, 6660-6667.

27. Thomas, L.; Byers, H.; Vink, J.; Stamenkovitch, I. *J. Cell. Biol.* **1992**, *118*, 971-980.

28. Bartozolli, A.; Peach, R.; Aruffo, A.; Stamenkovic, I. *J. Exp. Med.* **1994**, *180*, 53-66.

29. Turley, E.; Austen, L.; Vandeligt, K.; Clary, C. *J. Cell. Biol.* **1991**, *112*, 1041-1047.

30. Underhill, C. *J. Cell. Sci.* **1992**, *103*, 293-298.

31. Günthert, U.; Hofmann, M.; Rudy, W.; Reber, S.; Zöller, M.; Haußmann, I.; Matzku, S.; Wenzel, A.; Ponta, H.; Herrlich, P.; *Cell* **1991**, *65*, 13-24.

32. Assmann, V.; Kern, H. F.; Elsaesser, H. P. Clin. *Cancer Res.* **1996**, *2*, 1607-1618.

33. Gardner, M. J.; Catterall, J. B.; Jones, L. M. H.; Turner, G. A. *Clin. Exp. Metastasis* **1996**, *14*, 325-334.

34. Yeo, T. K.; Magy, J. A.; Yeo, K. T.; Dvorak, H. F.; Toole, B. P. *Am. J. Pathol.* **1996**, *148*, 1733-1740.

35. Wang, C.; Zhang, S.; Turley, E. A. *Round Table Ser.-R. Soc. Med. Press* **1996**, *45*, 37-53.

36. Mitchell, B. S.; Whitehouse, A.; Prehm, P.; Delpech, B.; Schumacher, U. *Clin Exp. Metastasis* **1996**, *56*, 107-114.

37. Lokeshwar, V. B.; Lokeshwar, B. L.; Pham, H. T.; Block, N. L. *Cancer Res.* **1996**, *56*, 651-657.

38. Laurent, U. B. G.; Laurent, T. C.; Hellsing, L. K.; Persson, L.; Hartman, M.; Lilja, K. *Acta Neurol. Scand.* **1996**, *94*, 194-206.

39. Jaworski, D. M.; Kelly, G. M.; Piepmeier, J. M.; Hockfield, S. *Cancer Res.* **1996**, *56*, 2293-2298.

40. Pauli, B.; Lee, C. *Lab. Invest.* **1988**, *58*, 379-387.

41. Zhu, D.; Cheng, C.; Pauli, B. *Proc. Natl. Acad. Sci. USA* **1991**, *88*, 9568-9572.

42. Zhu, D.; Cheng, C.; Pauli, B. *J. Clin. Invest.* **1992**, *89*, 1718-1724.

43. Cysyk, R. Unpublished results.

44. Rodén, L.; Campbell, P.; Fraser, J.; Laurent, T.; Pertoft, H.; Thompson, J. *The Biology of Hyaluronan;* Evered, D.; Whelan, J Eds.; Wiley: Chichester (Ciba Foundation Symposium, 143), **1989**, pp 60-86.

45. Fraser, J.; Laurent, T. *The Biology of Hyaluronan;* Evered, D.; Whelan, J Eds.; Wiley: Chichester (Ciba Foundation Symposium, 143), **1989**, pp 41-59.

46. McGuire, P.; Castellot, J.; Orkin, R. *J. Cell Physiol.* **1987**, *133*, 267.

47. Truppe, W.; Basner, R.; Figura, K.; Kresse, H. *Biochem. Biophys. Pes. Commun.* **1977**, *78*, 713.

48. Bernfield, M.; Banerjee, S. D.; Koda, J. E.; Rapraeger, A. C. *The Role of Extracellular Matrix in Development;* Trelstad, R.; Ed; Alan R. Liss: New York, **1984**, p 545.

49. Kresse, H.; Glössl, *J. Adv. Enzymol.* **1987**, *60*, 217-311.

50. Kishi, Y. *Pure Appl. Chem.* **1993**, *65*, 771-778.

51. Schmidt, R. R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21-123.

52. Fügedi, P.; Garegg, P. J.; Loen, H.; Norberg, T. *Glycoconjugate J.* **1987**, *4*, 97-108.

53. Hasegawa, A.; *ACS Symp. Ser.* **1994**, *560*, 184-197.

54. Sinnot, M. *Chem. Rev.* **1990**, *90*, 1171-1202.

55. Jiang, B. Ph. D. Dissertation, University of Tennessee, **1999**.

56. Martin, O.; Lai, W. *J. Org. Chem.* **1990**, *55*, 5188-5190.

57. Martin, O.; Lai, W. *J. Org. Chem.* **1993**, *58*, 176-185.

58. Postema, M. H. D. Calimente, D. *Tetrahedron Lett.* **1999**, *40*, 4755-4759.

59. Calimente, D.; Postema, M. H. D. *J. Org. Chem.* **1999**, *64*, 1770-1771.

60. Hoffmann, M.; Kessler, H. *Tetrahedron Lett.* **1994**, *35*, 6067-6070.

61. Hoffmann, M.; Burkhart, F.; Hessler, G.; Kessler, H. *Helv. Chim. Acta* **1996**, *79*, 1519-1532.

62. Hoffmann, M.; Kessler, H. *Tetrahedron Lett.* **1997**, *38*, 1903-1906.

63. Hamilton, S. Ph. D. Dissertation, University of Tennessee, **2001**.

64. Urban, D.; Skrydstrup, T. Beau, J.-M. *Chem. Commun.* **1998**, 955-956.

65. Urban, D.; Skrydstrup, T. Beau, J.-M. *J. Org. Chem.* **1998**, *63*, 2507-2516.

66. Price, N. K. Ph. D. Dissertation, University of Tennessee, **1997**.

67. Fukuyama, T.; Laud, A. A.; Hotchkiss, L. M. *Tetrahedron Lett.* **1985**, *26*, 6291.

68. Petiton, M.; Duchaussoy, P.; Choay, J. *Tetrahedron Lett.* **1988**, *29*, 1389.

69. Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190-6191.

70. Blanc-Muesser, M.; Driguez, H. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3345.

71. Schou, C.; Rasmussen, G.; Schulein, M.; Henrissat, B. Driguez, H. *J. Carbohydr. Chem.* **1993**, *12*, 743.

72. Wang, L.-X.; Lee, Y. C. *Carbohydr. Lett.* **1995**, *1*, 185.

73. Wang, L.-X.; Lee, Y. C. *J. Chem. Soc., Perkin Trans. 1*, **1995**, 581-591.

74. Auzanneau, F.; Bennis, K.; Fanton, E.; Prome, D.; Defaye, J.; Gelas, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3629-3635.

75. Pozsgay, V. *J. Am. Chem. Soc.* **1995**, *117*, 6673-6681.

76. Van Boom, J. H.; Burgers, P. M. J. *Tetrahedron Lett.* **1976**, 4875-4878.

77. Slaghek, T. M. Y.; Ogawa, N. T.; Kamerling, J. P.; Vliegenthart, J. F. G. *Carbohydr. Res.* **1994**, *255*, 61-85.

78. Aly, M. R. E.; Castro-Palomino, J. C.; Ibrahim, E.-S. I.; El-Ashry, E.-S. H.; Schmidt, R. R. *Eur. J. Org. Chem.* **1998**, 2305-2316.

79. Johansson, R.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. I* **1984**, 2371-2374.

80. Alzeer, J.; Cai, C.; Vasella, A. *Helv. Chim. Acta* **1995**, *78*, 242-264.

81. Ambrose, M. G.; Binkley, R. W. *J. Org. Chem.* **1983**, *48*, 674-677.

82. Horton, D. *Methods Carbohydr. Chem.*, **1972**, *6*, 282-285.

83. Mereyala, H. B.; Gurijala, V. R. *Carbohydr. Res.* **1993**, *242*, 277-280.

84. Hanessian, S.; Bacquet, C.; Lehong, N. *Carbohydr. Res.* **1980**, *80*, C17-C22.

85. Vasella, A.; Witzig, C.; Husi, R. *Helv. Chim. Acta* **1991**, *74*, 1362-1372.

86. Skrydstrup, T.; Jarreton, O.; Mazeas, D.; Urban, D.; Beau, J.-M. *Chem. Eur. J.* **1998**, *4*, 655-671.

87. Dietrich, H.; Schmidt, R. R. *Justus Liebigs Ann. Chem.* **1994**, 975-981.

88. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574-1585.

89. Oikawa, Y.; Yoshioka, T.; Youemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885.

90. Spijker, N. M.; Keuning, C. A.; Hooglugt, M.; Veeneman, G. H.; Van Boeckel, C. A. A. *Tetrahedron* **1996**, *52*, 5945-5960.

91. Toepfer, F.; Kinzy, W.; Schmidt, R. R. *Liebigs Ann. Chem.* **1994**, 449-464.

92. Paulsen, H.; Rutz, V.; Brockhausen, I. *Liebigs Ann. Chem.* **1992**, 747-758.

93. Yeung, B. K. S.; Hill, D. C.; Janicka, M.; Petillo, P. A. *Org.c Lett.* **2000**, *2*, 1279-1282.

94. Kochetkov, N. K.; Dmitriev, B. A.; Chernyak, A. Y.; Levinsky, A. B. *Carbohydr.*

Res. **1982**, *110*, C16-C20.

95. Sarbajna, S.; Roy, N. *Carbohydr. Res.* **1998**, *306*, 201-407.
96. Horton, D.; Wolfrom, M. L. *J. Org. Chem.* **1962**, *27*, 1794-1800.
97. Wang, L.; Yuan, C. *J. Chem. Soc., Perkin Trans. 1* **1995**, 581-591.
98. Eisele, T.; Schmidt, R. R. *Liebigs Ann. Recl.* **1997**, *5*, 865-872.
99. Hecker, S. J.; Minich, M. L.; Lackey, K. *J. Org. Chem.* **1990**, *55*, 4904-4911.
100. Ghavami, A.; Johnston, B. D.; Pinto, B. M. *J. Org. Chem.* **2001**, *66*, 2312-2317.
101. Yan, L.; Kahne, D. *Synlett* **1995**, 1157.
102. Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, 99.
103. Guindon, Y.; Yoakim, C.; Bernstein, M. A.; Morton, H. E. *Tetrahedron Lett.* **1985**, *26*, 1185.
104. Hummel, G.; Hindsgual, O. *Angew. Chem. Int. Ed.Engl* **1999**, *38*, 1782-1784.
105. Hindsgual, O.; Hummel, G. *PCT Intl.* Appl. No. WO 00 08038, **2000**.

APPENDICES

APPENDIX I. CRYSTAL DATA FOR COMPOUND 80A

Table 1. Crystal data and structure refinement for compound 80a.

Crystal data

$C_{57}H_{71}N\,O_{13}Si$

Mr = 1006.24

Monoclinic, $P2_1$

a = 5.8241(5) Å

b = 28.617(2) Å

c = 16.6076(14) Å

β = 96.207(2)°

V = 2751.7(4) Å^3

Z = 2

D_x = 1.214 Mg/m^3

Mo $K\alpha$ radiation

Cell parameters from 5069 reflections

θ = 1.88 to 26.41°

μ = 0.106 mm^{-1}

T = 295(2) K

Plate, colorless

0.42 × 0.35 × 0.05 mm^3

Data collection

Bruker SMART/CCD diffractometer

ω and ψ scans

Absorption correction: Semi-empirical from equivalents

T_{min} = 0.9570, T_{max} = 0.9947

25262 measured reflections

11016 independent reflections

6091 reflections with $I > 2\sigma(I)$

R_{int} = 0.0475

θ_{max} = 26.41°

h = -7→7

k = -35 →35

l = -20 → 20

Refinement

Refinement on F^2

R_1 = 0.0449

wR_2 = 0.0964

S = 0.983

11016 reflections

666 parameters

$R_1 = \Sigma\,||F_o| - |F_c||/\Sigma|F_o|$

$wR_2 = (\,\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[wF_o^2)^2]^{1/2}$

$(\Delta/\sigma)_{max}$ = 0.006

$\Delta\rho_{max}$ = 0.208 e.Å^{-3}

$\Delta\rho_{min}$ = 0.140 e.Å^{-3}

Absolute structure parameter = -0.06 (14)

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound 80a.

	x	y	z	U(eq)[a]
Si(1)	3152(1)	5063(1)	8264(1)	47(1)
O(4)	1287(3)	5123(1)	7447(1)	49(1)
O(5)	-2482(4)	4993(1)	2547(1)	55(1)
O(8)	-690(4)	6192(1)	3809(1)	52(1)
O(3)	-865(4)	4717(1)	5084(1)	52(1)
O(1)	3024(4)	4254(1)	6760(1)	53(1)
O(7)	1446(4)	5977(1)	2425(2)	67(1)
C(11)	1433(5)	5036(1)	6613(2)	43(1)
O(6)	-621(4)	5201(1)	1467(1)	62(1)
C(12)	-506(5)	5306(1)	6126(2)	47(1)
O(2)	2639(5)	3708(1)	5706(2)	78(1)
C(23)	-2520(5)	5431(1)	3782(2)	44(1)
C(22)	-2523(5)	5466(1)	4707(2)	46(1)
C(10)	1139(5)	4523(1)	6387(2)	46(1)
C(27)	-530(5)	5724(1)	3513(2)	46(1)
C(24)	-2381(5)	4941(1)	3413(2)	46(1)
C(9)	1037(6)	4465(1)	5477(2)	52(1)
C(13)	-592(6)	5209(1)	5215(2)	44(1)
C(26)	-546(6)	5727(1)	2593(2)	50(1)
C(51)	-229(6)	4751(1)	1174(2)	50(1)
O(9)	-4746(4)	5324(1)	4919(2)	62(1)
O(13)	-3681(4)	4172(1)	3250(2)	83(1)
C(25)	-525(6)	5222(1)	2320(2)	51(1)
C(28)	-4296(6)	4611(1)	3565(2)	58(1)
C(1)	4749(7)	3506(1)	6973(3)	65(1)
C(53)	2170(6)	4097(1)	985(2)	62(1)

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound 80a (cont'd).

	x	y	z	U(eq)[a]
C(54)	408(7)	3887(1)	498(2)	60(1)
C(7)	2725(6)	3774(1)	6547(2)	61(1)
O(11)	526(5)	3457(1)	135(2)	87(1)
C(37)	1437(6)	6386(1)	4157(3)	69(1)
C(38)	1042(7)	6829(1)	4587(2)	66(1)
C(8)	770(7)	3952(1)	5278(2)	74(1)
C(30)	-4603(7)	3412(1)	2773(3)	67(1)
C(29)	-5297(7)	3816(1)	3257(3)	75(1)
C(34)	-2142(8)	3069(2)	1862(3)	83(1)
C(56)	-2002(6)	4546(1)	686(2)	64(1)
C(5)	7813(8)	2947(2)	6991(4)	94(2)
C(44)	1325(8)	6199(2)	1643(3)	84(1)
C(52)	1842(6)	4535(1)	1311(2)	61(1)
C(48)	-4231(10)	7183(2)	1142(4)	103(2)
C(45)	-648(8)	6543(1)	1477(3)	73(1)
C(32)	-5240(9)	2628(2)	2277(3)	94(2)
O(12)	-2989(8)	2275(1)	1381(3)	122(1)
C(55)	-1679(7)	4112(1)	348(2)	69(1)
C(46)	-1830(10)	6584(2)	714(3)	94(2)
C(49)	-3082(10)	7147(2)	1906(4)	94(2)
C(39)	-940(9)	7078(2)	4469(3)	93(1)
C(35)	-2748(7)	3434(1)	2328(3)	77(1)
C(33)	-3411(9)	2660(2)	1834(3)	86(1)
C(41)	579(18)	7664(2)	5387(5)	135(3)
C(2)	5363(9)	3572(2)	7778(3)	106(2)
C(57)	2694(9)	3246(2)	123(4)	113(2)

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound 80a (cont'd).

	x	y	z	U(eq)[a]
C(43)	2774(10)	7005(2)	5109(4)	132(2)
C(6)	5979(7)	3189(2)	6573(3)	82(1)
C(4)	8401(8)	3020(2)	7788(4)	93(1)
C(50)	-1336(9)	6835(2)	2068(3)	87(1)
C(40)	-1145(13)	7503(2)	4894(4)	121(2)
C(31)	-5837(8)	2995(2)	2731(3)	86(1)
C(47)	-3568(11)	6907(2)	549(4)	116(2)
C(36)	-1153(12)	2303(2)	870(5)	142(2)
C(3)	7203(10)	3337(2)	8180(3)	113(2)
C(42)	2511(16)	7425(3)	5512(5)	178(4)
O(10)	-4128(7)	5935(1)	6272(2)	93(1)
N(1)	-296(6)	5803(1)	6313(2)	66(1)
C(19)	3102(5)	5632(1)	8832(2)	57(1)
C(15)	2131(6)	4581(1)	8871(2)	68(1)
C(16)	4405(7)	5583(2)	9688(2)	84(1)
C(14)	6079(5)	4941(1)	7988(2)	68(1)
C(20)	-2124(11)	6079(2)	6417(2)	78(1)
C(18)	4196(7)	6024(1)	8364(3)	78(1)
C(17)	589(6)	5774(2)	8914(3)	95(2)
C(21)	-1556(12)	6562(2)	6715(3)	131(2)

Table 3. Bond lengths [Å] and angles [°] for compound 80a.[b]

Si(1)-O(4)	1.653(2)	Si(1)-C(15)	1.843(4)
Si(1)-C(14)	1.845(3)	Si(1)-C(19)	1.885(4)
O(4)-C(11)	1.419(3)	O(5)-C(25)	1.402(4)
O(5)-C(24)	1.440(3)	O(8)-C(37)	1.422(4)
O(8)-C(27)	1.434(4)	O(3)-C(9)	1.421(4)
O(3)-C(13)	1.430(4)	O(1)-C(7)	1.424(4)
O(1)-C(10)	1.427(3)	O(7)-C(26)	1.416(4)
O(7)-C(44)	1.441(5)	C(11)-C(10)	1.520(4)
C(11)-C(12)	1.527(4)	O(6)-C(51)	1.402(4)
O(6)-C(25)	1.413(4)	C(12)-N(1)	1.458(4)
C(12)-C(13)	1.533(4)	O(2)-C(7)	1.405(4)
O(2)-C(8)	1.418(4)	C(23)-C(22)	1.539(4)
C(23)-C(24)	1.537(4)	C(23)-C(27)	1.535(4)
C(22)-O(9)	1.437(3)	C(22)-C(13)	1.522(4)
C(10)-C(9)	1.514(4)	C(27)-C(26)	1.527(4)
C(24)-C(28)	1.502(4)	C(9)-C(8)	1.508(5)
C(26)-C(25)	1.515(4)	C(51)-C(52)	1.353(5)
C(51)-C(56)	1.375(5)	O(13)-C(29)	1.389(4)
O(13)-C(28)	1.423(4)	C(1)-C(2)	1.358(6)
C(1)-C(6)	1.370(5)	C(1)-C(7)	1.516(5)
C(53)-C(54)	1.375(5)	C(53)-C(52)	1.386(5)
C(54)-C(55)	1.375(5)	C(54)-O(11)	1.375(4)
O(11)-C(57)	1.401(5)	C(37)-C(38)	1.485(5)
C(38)-C(39)	1.353(6)	C(38)-C(43)	1.355(6)
C(30)-C(35)	1.374(5)	C(30)-C(31)	1.391(5)
C(30)-C(29)	1.486(5)	C(34)-C(35)	1.368(6)
C(34)-C(33)	1.382(6)	C(56)-C(55)	1.382(5)
C(5)-C(4)	1.348(6)	C(5)-C(6)	1.395(6)

Table 3. Bond lengths [Å] and angles [°] for compound 80a (cont'd).[b]

C(44)-C(45)	1.516(6)	C(48)-C(47)	1.351(8)
C(48)-C(49)	1.374(7)	C(45)-C(50)	1.380(6)
C(45)-C(46)	1.379(6)	C(32)-C(33)	1.360(7)
C(32)-C(31)	1.359(6)	O(12)-C(33)	1.371(6)
O(12)-C(36)	1.437(7)	C(46)-C(47)	1.376(7)
C(49)-C(50)	1.359(6)	C(39)-C(40)	1.420(7)
C(41)-C(40)	1.309(8)	C(41)-C(42)	1.315(9)
C(2)-C(3)	1.377(6)	C(43)-C(42)	1.391(9)
C(4)-C(3)	1.353(6)	O(10)-C(20)	1.237(5)
N(1)-C(20)	1.351(6)	C(19)-C(16)	1.543(5)
C(19)-C(17)	1.539(5)	C(19)-C(18)	1.542(5)
C(20)-C(21)	1.493(6)	O(4)-Si(1)-C(14)	111.04(14)
O(4)-Si(1)-C(15)	107.78(15)	O(4)-Si(1)-C(19)	106.06(14)
C(15)-Si(1)-C(14)	110.86(18)	C(14)-Si(1)-C(19)	110.61(16)
C(15)-Si(1)-C(19)	110.35(17)	C(25)-O(5)-C(24)	111.8(2)
C(11)-O(4)-Si(1)	132.80(17)	C(9)-O(3)-C(13)	111.2(2)
C(37)-O(8)-C(27)	114.7(2)	C(26)-O(7)-C(44)	116.1(3)
C(7)-O(1)-C(10)	110.2(2)	O(4)-C(11)-C(12)	108.0(2)
O(4)-C(11)-C(10)	113.2(2)	C(51)-O(6)-C(25)	113.4(2)
C(10)-C(11)-C(12)	107.6(2)	N(1)-C(12)-C(13)	112.4(3)
N(1)-C(12)-C(11)	110.0(3)	C(7)-O(2)-C(8)	112.0(3)
C(11)-C(12)-C(13)	111.9(2)	C(22)-C(23)-C(27)	109.7(3)
C(22)-C(23)-C(24)	117.7(3)	O(9)-C(22)-C(13)	111.0(3)
C(24)-C(23)-C(27)	107.9(2)	C(13)-C(22)-C(23)	116.2(3)
O(9)-C(22)-C(23)	108.9(2)	O(1)-C(10)-C(9)	108.6(2)
O(1)-C(10)-C(11)	110.7(2)	O(8)-C(27)-C(26)	110.0(2)
C(11)-C(10)-C(9)	110.1(2)	C(26)-C(27)-C(23)	111.8(3)
O(8)-C(27)-C(23)	109.3(2)	O(5)-C(24)-C(23)	107.9(2)

Table 3. Bond lengths [Å] and angles [°] for compound 80a (cont'd).[b]

O(5)-C(24)-C(28)	106.4(2)	O(3)-C(9)-C(8)	109.7(3)
C(28)-C(24)-C(23)	115.7(3)	C(8)-C(9)-C(10)	108.5(3)
O(3)-C(9)-C(10)	110.3(3)	O(3)-C(13)-C(12)	108.7(2)
O(3)-C(13)-C(22)	109.2(3)	O(7)-C(26)-C(25)	112.9(3)
C(22)-C(13)-C(12)	113.7(3)	C(25)-C(26)-C(27)	107.1(3)
O(7)-C(26)-C(27)	106.5(3)	C(52)-C(51)-O(6)	122.5(3)
C(52)-C(51)-C(56)	120.1(3)	C(29)-O(13)-C(28)	116.6(3)
C(56)-C(51)-O(6)	117.2(3)	O(5)-C(25)-C(26)	109.5(3)
O(5)-C(25)-O(6)	107.7(2)	O(13)-C(28)-C(24)	105.7(3)
O(6)-C(25)-C(26)	109.9(3)	C(2)-C(1)-C(7)	119.8(4)
C(2)-C(1)-C(6)	118.3(4)	C(54)-C(53)-C(52)	120.0(3)
C(6)-C(1)-C(7)	121.9(4)	C(55)-C(54)-C(53)	119.3(3)
C(55)-C(54)-O(11)	115.2(3)	O(2)-C(7)-O(1)	111.5(3)
O(11)-C(54)-C(53)	125.4(3)	O(1)-C(7)-C(1)	107.7(3)
O(2)-C(7)-C(1)	109.8(3)	O(8)-C(37)-C(38)	110.8(3)
C(54)-O(11)-C(57)	118.6(3)	C(39)-C(38)-C(37)	123.6(4)
C(39)-C(38)-C(43)	117.5(5)	O(2)-C(8)-C(9)	108.3(3)
C(43)-C(38)-C(37)	118.9(4)	C(35)-C(30)-C(29)	122.1(3)
C(35)-C(30)-C(31)	116.2(4)	O(13)-C(29)-C(30)	110.0(3)
C(31)-C(30)-C(29)	121.6(4)	C(51)-C(56)-C(55)	119.8(3)
C(35)-C(34)-C(33)	119.7(4)	O(7)-C(44)-C(45)	114.4(3)
C(4)-C(5)-C(6)	120.7(4)	C(47)-C(48)-C(49)	118.7(6)
C(51)-C(52)-C(53)	120.4(3)	C(50)-C(45)-C(44)	122.3(4)
C(50)-C(45)-C(46)	116.7(5)	C(33)-C(32)-C(31)	120.7(4)
C(46)-C(45)-C(44)	121.0(4)	C(54)-C(55)-C(56)	120.3(4)
C(33)-O(12)-C(36)	118.0(4)	C(50)-C(49)-C(48)	120.8(5)
C(47)-C(46)-C(45)	121.5(5)	C(34)-C(35)-C(30)	122.4(4)
C(38)-C(39)-C(40)	119.7(5)	C(32)-C(33)-C(34)	119.0(5)

Table 3. Bond lengths [Å] and angles [°] for compound 80a (cont'd).[b]

C(32)-C(33)-O(12)	116.1(4)	C(40)-C(41)-C(42)	120.0(7)
O(12)-C(33)-C(34)	124.8(5)	C(38)-C(43)-C(42)	121.1(6)
C(1)-C(2)-C(3)	121.2(4)	C(3)-C(4)-C(5)	119.2(4)
C(1)-C(6)-C(5)	120.0(4)	C(41)-C(40)-C(39)	120.9(6)
C(49)-C(50)-C(45)	121.7(5)	C(48)-C(47)-C(46)	120.7(6)
C(32)-C(31)-C(30)	121.9(4)	C(41)-C(42)-C(43)	120.8(7)
C(4)-C(3)-C(2)	120.6(5)	C(16)-C(19)-C(17)	108.7(3)
C(20)-N(1)-C(12)	123.3(4)	C(17)-C(19)-C(18)	107.5(3)
C(16)-C(19)-C(18)	109.9(3)	C(17)-C(19)-Si(1)	109.8(2)
C(16)-C(19)-Si(1)	110.6(3)	O(10)-C(20)-N(1)	121.3(4)
C(18)-C(19)-Si(1)	110.3(2)	N(1)-C(20)-C(21)	115.7(5)
O(10)-C(20)-C(21)	123.0(5)		

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for compound 80a.[c]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	38(1)	62(1)	43(1)	-1(1)	7(1)	3(1)
O(4)	45(1)	66(1)	37(1)	0(1)	7(1)	10(1)
O(5)	64(1)	60(2)	39(1)	2(1)	5(1)	-7(1)
O(8)	55(1)	50(1)	49(1)	-1(1)	5(1)	-2(1)
O(3)	59(1)	49(1)	47(1)	-2(1)	-1(1)	1(1)
O(1)	58(1)	46(1)	54(1)	1(1)	1(1)	9(1)
O(7)	77(2)	70(2)	60(2)	3(1)	28(1)	-14(1)
C(11)	45(2)	52(2)	34(2)	-2(2)	12(1)	2(2)
O(6)	87(2)	59(2)	40(1)	4(1)	12(1)	6(1)
C(12)	57(2)	42(2)	42(2)	-1(2)	8(2)	1(2)
O(2)	108(2)	55(2)	65(2)	-9(1)	-8(2)	21(1)
C(23)	43(2)	50(2)	40(2)	4(2)	7(2)	3(2)
C(22)	45(2)	49(2)	45(2)	1(2)	10(2)	5(1)
C(10)	47(2)	47(2)	44(2)	6(2)	8(2)	2(2)
C(27)	48(2)	48(2)	43(2)	3(2)	8(2)	1(1)
C(24)	50(2)	54(2)	35(2)	1(2)	4(1)	-4(2)
C(9)	58(2)	48(2)	49(2)	-2(2)	2(2)	6(2)
C(13)	46(2)	46(2)	41(2)	3(2)	10(2)	-2(1)
C(26)	54(2)	49(2)	48(2)	2(2)	13(2)	-3(2)
C(51)	62(2)	54(2)	37(2)	1(2)	12(2)	-1(2)
O(9)	42(1)	84(2)	62(2)	7(1)	20(1)	4(1)
O(13)	83(2)	64(2)	106(2)	-20(2)	29(2)	-25(1)
C(25)	57(2)	61(2)	37(2)	3(2)	10(2)	0(2)
C(28)	53(2)	64(2)	58(2)	-3(2)	9(2)	-11(2)
C(1)	82(3)	47(2)	65(3)	2(2)	4(2)	7(2)
C(53)	63(2)	74(3)	49(2)	0(2)	4(2)	13(2)
C(54)	71(2)	50(2)	59(2)	-3(2)	10(2)	-2(2)

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for compound 80a (cont'd).[c]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(7)	73(2)	45(2)	62(3)	1(2)	0(2)	8(2)
O(11)	98(2)	60(2)	102(2)	-22(2)	10(2)	0(2)
C(37)	61(2)	68(3)	77(3)	-14(2)	2(2)	-5(2)
C(38)	80(3)	58(2)	58(3)	-1(2)	3(2)	-9(2)
C(8)	100(3)	56(2)	61(3)	-5(2)	-14(2)	14(2)
C(30)	73(2)	54(2)	72(3)	8(2)	-3(2)	-11(2)
C(29)	70(2)	68(3)	87(3)	13(2)	14(2)	-21(2)
C(34)	89(3)	61(3)	99(4)	-11(2)	12(3)	-17(2)
C(56)	55(2)	76(3)	61(2)	7(2)	3(2)	8(2)
C(5)	88(3)	83(3)	112(4)	-10(3)	15(3)	32(3)
C(44)	118(3)	76(3)	67(3)	7(2)	47(3)	-14(3)
C(52)	57(2)	77(3)	50(2)	-12(2)	5(2)	-1(2)
C(48)	123(4)	78(4)	109(5)	10(3)	13(4)	-9(3)
C(45)	115(3)	51(2)	58(3)	8(2)	31(3)	-18(2)
C(32)	126(4)	56(3)	98(4)	4(3)	8(3)	-34(3)
O(12)	171(4)	63(2)	134(3)	-26(2)	28(3)	-30(2)
C(55)	65(2)	65(3)	76(3)	-14(2)	-1(2)	-7(2)
C(46)	124(4)	99(4)	62(3)	-8(3)	23(3)	-20(3)
C(49)	140(4)	53(3)	92(4)	0(3)	19(4)	-4(3)
C(39)	113(3)	72(3)	91(4)	-9(3)	-6(3)	16(3)
C(35)	79(3)	54(2)	101(3)	-5(2)	17(3)	-21(2)
C(33)	110(3)	57(3)	89(3)	3(3)	1(3)	-14(3)
C(41)	215(9)	72(4)	120(5)	-31(4)	25(6)	-20(5)
C(2)	150(4)	93(3)	71(3)	-4(3)	-7(3)	71(3)
C(57)	122(4)	74(3)	147(5)	-25(3)	29(4)	14(3)
C(43)	109(4)	127(5)	152(6)	-71(4)	-21(4)	-2(3)

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for compound 80a (cont'd).[c]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(6)	88(3)	73(3)	83(3)	-15(2)	3(2)	16(2)
C(4)	100(3)	73(3)	103(4)	6(3)	-6(3)	27(3)
C(50)	138(4)	62(3)	62(3)	0(2)	14(3)	0(3)
C(40)	166(6)	82(4)	117(5)	-3(4)	27(5)	31(4)
C(31)	95(3)	75(3)	87(3)	18(3)	5(3)	-32(2)
C(47)	128(5)	125(5)	89(4)	9(4)	-11(4)	-11(4)
C(36)	157(5)	95(4)	177(7)	-46(4)	34(5)	-5(4)
C(3)	153(5)	96(4)	82(4)	-6(3)	-18(3)	56(4)
C(42)	187(8)	144(7)	190(8)	-102(6)	-40(6)	-17(6)
O(10)	121(3)	96(2)	65(2)	1(2)	23(2)	52(2)
N(1)	96(2)	47(2)	52(2)	-1(2)	3(2)	8(2)
C(19)	43(2)	71(2)	58(2)	-15(2)	11(2)	-2(2)
C(15)	64(2)	85(3)	55(2)	16(2)	6(2)	2(2)
C(16)	78(3)	112(4)	61(3)	-18(2)	4(2)	-15(2)
C(14)	48(2)	88(3)	69(2)	-16(2)	11(2)	5(2)
C(20)	132(4)	56(3)	46(2)	2(2)	6(3)	24(3)
C(18)	71(2)	67(3)	96(3)	-10(2)	6(2)	-2(2)
C(17)	51(2)	111(4)	125(4)	-59(3)	18(2)	2(2)
C(21)	238(7)	63(3)	90(4)	-12(3)	7(4)	46(4)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2$ $\times 10^3$) for compound 80a.

	x	y	z	U(eq)
H(11)	2927	5146	6468	52
H(12)	-1969	5198	6301	56
H(22)	-2351	5798	4846	55
H(10)	-302	4407	6568	55
H(27)	933	5588	3751	56
H(24)	-900	4799	3615	56
H(9)	2474	4581	5292	63
H(26)	-1939	5884	2342	60
H(9A)	-4988	5448	5347	93
H(25)	878	5067	2566	62
H(28A)	-4433	4588	4140	70
H(28B)	-5757	4719	3292	70
H(53)	3583	3946	1095	75
H(7)	1288	3659	6733	73
H(37A)	2427	6445	3735	83
H(37B)	2214	6164	4535	83
H(8A)	-683	3837	5436	89
H(8B)	774	3904	4700	89
H(29A)	-6801	3928	3031	90
H(29B)	-5410	3717	3810	90
H(34)	-883	3096	1566	99
H(56)	-3415	4697	584	77
H(5)	8640	2732	6717	113
H(44A)	1172	5960	1228	101
H(44B)	2767	6362	1601	101
H(52)	3052	4680	1627	73

Table 5. Hydrogen coordinates (× 10^4) and isotropic displacement parameters (Å^2 × 10^3) for compound 80a (cont'd).

	x	y	z	U(eq)
H(48)	-5441	7394	1034	124
H(32)	-6090	2353	2268	112
H(55)	-2878	3973	17	83
H(46)	-1444	6388	302	113
H(49)	-3504	7339	2318	113
H(39)	-2165	6970	4111	112
H(35)	-1873	3706	2345	93
H(41)	437	7948	5650	162
H(2)	4525	3781	8061	128
H(57A)	3693	3452	-134	170
H(57B)	2523	2958	-173	170
H(57C)	3350	3185	668	170
H(43)	4161	6843	5200	158
H(6)	5590	3136	6023	98
H(4)	9616	2855	8066	112
H(50)	-586	6817	2591	104
H(40)	-2522	7670	4821	145
H(31)	-7107	2966	3022	103
H(47)	-4294	6935	25	139
H(36A)	-1392	2569	519	213
H(36B)	-1139	2024	550	213
H(36C)	297	2334	1200	213
H(3)	7627	3396	8727	135
H(42)	3716	7537	5873	214
H(1)	1058	5927	6360	79
H(15A)			898	

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2$ $\times 10^3$) for compound 80a (cont'd).

	x	y	z	U(eq)
H(15B)	3381	4473	9249	102
H(15C)	1582	4330	8520	102
H(16A)	4352	5875	9971	126
H(16B)	5984	5500	9645	126
H(16C)	3690	5344	9981	126
H(14A)	6066	4653	7691	102
H(14B)	7136	4915	8472	102
H(14C)	6558	5191	7659	102
H(18A)	3367	6054	7835	117
H(18B)	5780	5948	8314	117
H(18C)	4124	6313	8653	117
H(17A)	-158	5531	9186	143
H(17B)	-218	5822	8385	143
H(17C)	574	6058	9220	143
H(21A)	-2423	6785	6372	197
H(21B)	66	6619	6705	197
H(21C)	-1945	6594	7259	197
H(13)	870(50)	5295(10)	5025(17)	42(8)
H(23)	-4040(50)	5583(10)	3555(17)	41(8)

Table 6. Torsion angles [°] for compound 80a.[b]

C(15)-Si(1)-O(4)-C(11)	-111.2(3)
C(14)-Si(1)-O(4)-C(11)	10.4(3)
C(19)-Si(1)-O(4)-C(11)	130.6(3)
Si(1)-O(4)-C(11)-C(10)	79.8(3)
Si(1)-O(4)-C(11)-C(12)	-161.2(2)
O(4)-C(11)-C(12)-N(1)	58.0(3)
C(10)-C(11)-C(12)-N(1)	-179.5(2)
O(4)-C(11)-C(12)-C(13)	-176.2(2)
C(10)-C(11)-C(12)-C(13)	-53.7(3)
C(24)-C(23)-C(22)-O(9)	-74.5(3)
C(27)-C(23)-C(22)-O(9)	161.7(2)
C(24)-C(23)-C(22)-C(13)	51.6(4)
C(27)-C(23)-C(22)-C(13)	-72.2(4)
C(7)-O(1)-C(10)-C(11)	179.7(3)
C(7)-O(1)-C(10)-C(9)	-59.3(3)
O(4)-C(11)-C(10)-O(1)	-66.5(3)
C(12)-C(11)-C(10)-O(1)	174.3(2)
O(4)-C(11)-C(10)-C(9)	173.5(2)
C(12)-C(11)-C(10)-C(9)	54.3(3)
C(37)-O(8)-C(27)-C(26)	-101.6(3)
C(37)-O(8)-C(27)-C(23)	135.1(3)
C(22)-C(23)-C(27)-O(8)	-54.0(3)
C(24)-C(23)-C(27)-O(8)	176.6(2)
C(22)-C(23)-C(27)-C(26)	-176.2(3)
C(24)-C(23)-C(27)-C(26)	54.5(3)
C(25)-O(5)-C(24)-C(28)	-168.9(3)
C(25)-O(5)-C(24)-C(23)	66.4(3)
C(22)-C(23)-C(24)-O(5)	178.1(2)

Table 6. Torsion angles [°] for compound 80a (cont'd).[b]

C(27)-C(23)-C(24)-O(5)	-57.2(3)
C(22)-C(23)-C(24)-C(28)	59.2(4)
C(27)-C(23)-C(24)-C(28)	-176.1(3)
C(13)-O(3)-C(9)-C(8)	-176.1(3)
C(13)-O(3)-C(9)-C(10)	64.4(3)
O(1)-C(10)-C(9)-O(3)	178.3(2)
C(11)-C(10)-C(9)-O(3)	-60.4(3)
O(1)-C(10)-C(9)-C(8)	58.1(3)
C(11)-C(10)-C(9)-C(8)	179.4(3)
C(9)-O(3)-C(13)-C(22)	173.6(2)
C(9)-O(3)-C(13)-C(12)	-61.7(3)
O(9)-C(22)-C(13)-O(3)	59.5(3)
C(23)-C(22)-C(13)-O(3)	-65.6(3)
O(9)-C(22)-C(13)-C(12)	-62.1(4)
C(23)-C(22)-C(13)-C(12)	172.8(3)
N(1)-C(12)-C(13)-O(3)	-178.3(3)
C(11)-C(12)-C(13)-O(3)	57.3(3)
N(1)-C(12)-C(13)-C(22)	-56.4(4)
C(11)-C(12)-C(13)-C(22)	179.2(3)
C(44)-O(7)-C(26)-C(25)	88.7(4)
C(44)-O(7)-C(26)-C(27)	-154.0(3)
O(8)-C(27)-C(26)-O(7)	62.4(3)
C(23)-C(27)-C(26)-O(7)	-175.8(2)
O(8)-C(27)-C(26)-C(25)	-176.5(2)
C(23)-C(27)-C(26)-C(25)	-54.8(3)
C(25)-O(6)-C(51)-C(52)	-67.1(4)
C(25)-O(6)-C(51)-C(56)	117.2(3)
C(24)-O(5)-C(25)-O(6)	172.2(2)

Table 6. Torsion angles [°] for compound 80a (cont'd).[b]

C(24)-O(5)-C(25)-C(26)	-68.3(3)
C(51)-O(6)-C(25)-O(5)	-70.7(3)
C(51)-O(6)-C(25)-C(26)	170.1(3)
O(7)-C(26)-C(25)-O(5)	176.7(2)
C(27)-C(26)-C(25)-O(5)	59.8(3)
O(7)-C(26)-C(25)-O(6)	-65.2(3)
C(27)-C(26)-C(25)-O(6)	177.9(2)
C(29)-O(13)-C(28)-C(24)	-174.6(3)
O(5)-C(24)-C(28)-O(13)	66.5(3)
C(23)-C(24)-C(28)-O(13)	-173.8(3)
C(52)-C(53)-C(54)-C(55)	-0.7(6)
C(52)-C(53)-C(54)-O(11)	179.4(3)
C(8)-O(2)-C(7)-O(1)	-60.7(4)
C(8)-O(2)-C(7)-C(1)	-180.0(3)
C(10)-O(1)-C(7)-O(2)	60.6(4)
C(10)-O(1)-C(7)-C(1)	-178.9(3)
C(2)-C(1)-C(7)-O(2)	170.6(4)
C(6)-C(1)-C(7)-O(2)	-10.4(5)
C(2)-C(1)-C(7)-O(1)	49.0(5)
C(6)-C(1)-C(7)-O(1)	-132.0(4)
C(55)-C(54)-O(11)-C(57)	167.5(4)
C(53)-C(54)-O(11)-C(57)	-12.6(6)
C(27)-O(8)-C(37)-C(38)	-168.9(3)
O(8)-C(37)-C(38)-C(39)	-17.3(6)
O(8)-C(37)-C(38)-C(43)	164.8(5)
C(7)-O(2)-C(8)-C(9)	58.6(4)
O(3)-C(9)-C(8)-O(2)	-177.6(3)
C(10)-C(9)-C(8)-O(2)	-57.0(4)

Table 6. Torsion angles [°] for compound 80a (cont'd).[b]

C(28)-O(13)-C(29)-C(30)	169.4(3)
C(35)-C(30)-C(29)-O(13)	-6.4(6)
C(31)-C(30)-C(29)-O(13)	175.2(4)
C(52)-C(51)-C(56)-C(55)	1.2(5)
O(6)-C(51)-C(56)-C(55)	176.9(3)
C(26)-O(7)-C(44)-C(45)	57.5(4)
C(56)-C(51)-C(52)-C(53)	-2.2(5)
O(6)-C(51)-C(52)-C(53)	-177.7(3)
C(54)-C(53)-C(52)-C(51)	1.9(5)
O(7)-C(44)-C(45)-C(50)	38.0(5)
O(7)-C(44)-C(45)-C(46)	-142.9(4)
O(11)-C(54)-C(55)-C(56)	179.6(3)
C(53)-C(54)-C(55)-C(56)	-0.3(6)
C(51)-C(56)-C(55)-C(54)	0.1(6)
C(50)-C(45)-C(46)-C(47)	1.6(7)
C(44)-C(45)-C(46)-C(47)	-177.6(4)
C(47)-C(48)-C(49)-C(50)	-1.0(8)
C(43)-C(38)-C(39)-C(40)	-0.7(8)
C(37)-C(38)-C(39)-C(40)	-178.6(4)
C(33)-C(34)-C(35)-C(30)	-0.5(7)
C(31)-C(30)-C(35)-C(34)	0.5(6)
C(29)-C(30)-C(35)-C(34)	-177.9(4)
C(31)-C(32)-C(33)-O(12)	-178.4(4)
C(31)-C(32)-C(33)-C(34)	0.9(7)
C(36)-O(12)-C(33)-C(32)	176.6(5)
C(36)-O(12)-C(33)-C(34)	-2.6(8)
C(35)-C(34)-C(33)-C(32)	-0.3(7)
C(35)-C(34)-C(33)-O(12)	179.0(4)

Table 6. Torsion angles [°] for compound 80a (cont'd).[b]

C(6)-C(1)-C(2)-C(3)	1.4(8)
C(7)-C(1)-C(2)-C(3)	-179.5(5)
C(39)-C(38)-C(43)-C(42)	0.4(9)
C(37)-C(38)-C(43)-C(42)	178.4(6)
C(2)-C(1)-C(6)-C(5)	-0.3(7)
C(7)-C(1)-C(6)-C(5)	-179.3(4)
C(4)-C(5)-C(6)-C(1)	-0.1(7)
C(6)-C(5)-C(4)-C(3)	-0.7(8)
C(48)-C(49)-C(50)-C(45)	0.1(7)
C(46)-C(45)-C(50)-C(49)	-0.4(6)
C(44)-C(45)-C(50)-C(49)	178.8(4)
C(42)-C(41)-C(40)-C(39)	-1.9(12)
C(38)-C(39)-C(40)-C(41)	1.4(9)
C(33)-C(32)-C(31)-C(30)	-0.9(8)
C(35)-C(30)-C(31)-C(32)	0.1(6)
C(29)-C(30)-C(31)-C(32)	178.6(4)
C(49)-C(48)-C(47)-C(46)	2.2(8)
C(45)-C(46)-C(47)-C(48)	-2.6(8)
C(5)-C(4)-C(3)-C(2)	1.8(9)
C(1)-C(2)-C(3)-C(4)	-2.3(9)
C(40)-C(41)-C(42)-C(43)	1.6(14)
C(38)-C(43)-C(42)-C(41)	-0.8(13)
C(11)-C(12)-N(1)-C(20)	-138.6(3)
C(13)-C(12)-N(1)-C(20)	96.0(4)
O(4)-Si(1)-C(19)-C(16)	168.7(2)
C(15)-Si(1)-C(19)-C(16)	52.2(3)
C(14)-Si(1)-C(19)-C(16)	-70.8(3)
O(4)-Si(1)-C(19)-C(17)	48.7(3)

Table 6. Torsion angles [°] for compound 80a (cont'd).[b]

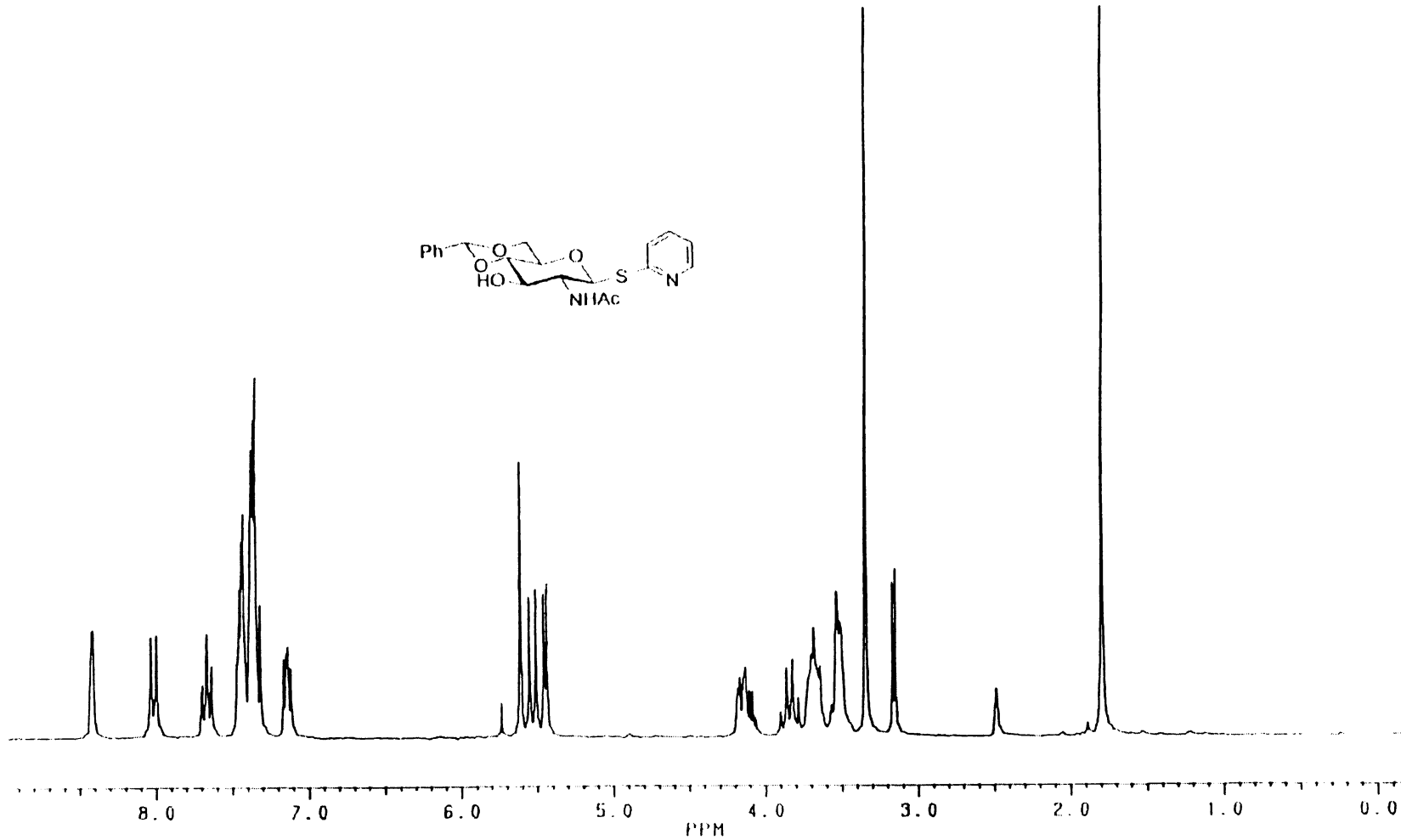
C(15)-Si(1)-C(19)-C(17)	-67.7(3)
C(14)-Si(1)-C(19)-C(17)	169.2(3)
O(4)-Si(1)-C(19)-C(18)	-69.5(3)
C(15)-Si(1)-C(19)-C(18)	174.0(2)
C(14)-Si(1)-C(19)-C(18)	51.0(3)
C(12)-N(1)-C(20)-O(10)	-7.9(6)
C(12)-N(1)-C(20)-C(21)	172.0(4)

[a] U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

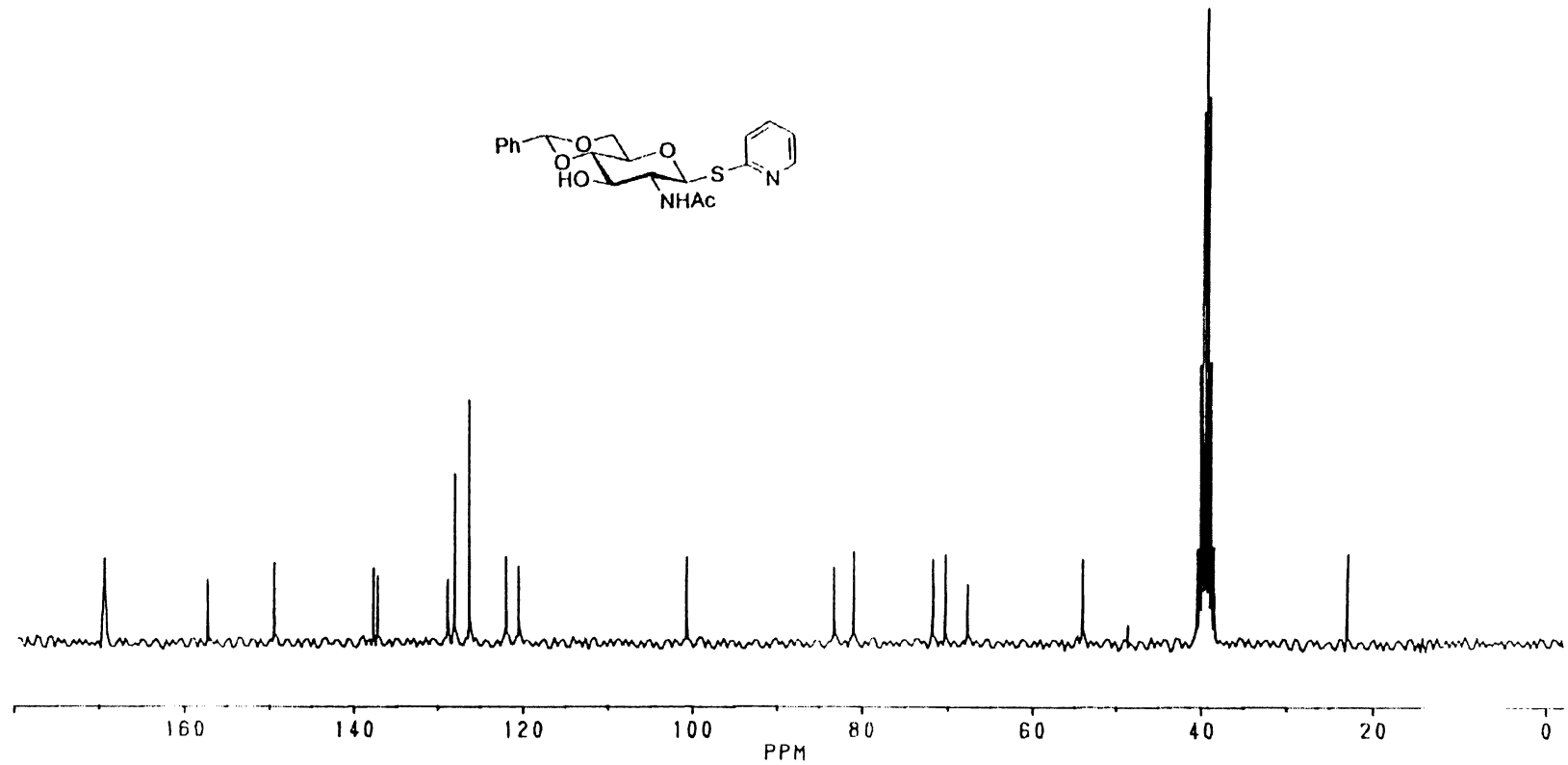
[b] Symmetry transformations used to generate equivalent atoms.

[c] The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2\, a^{*2}U^{11} + \ldots + 2\, h\, k\, a^*\, b^*\, U^{12}]$.

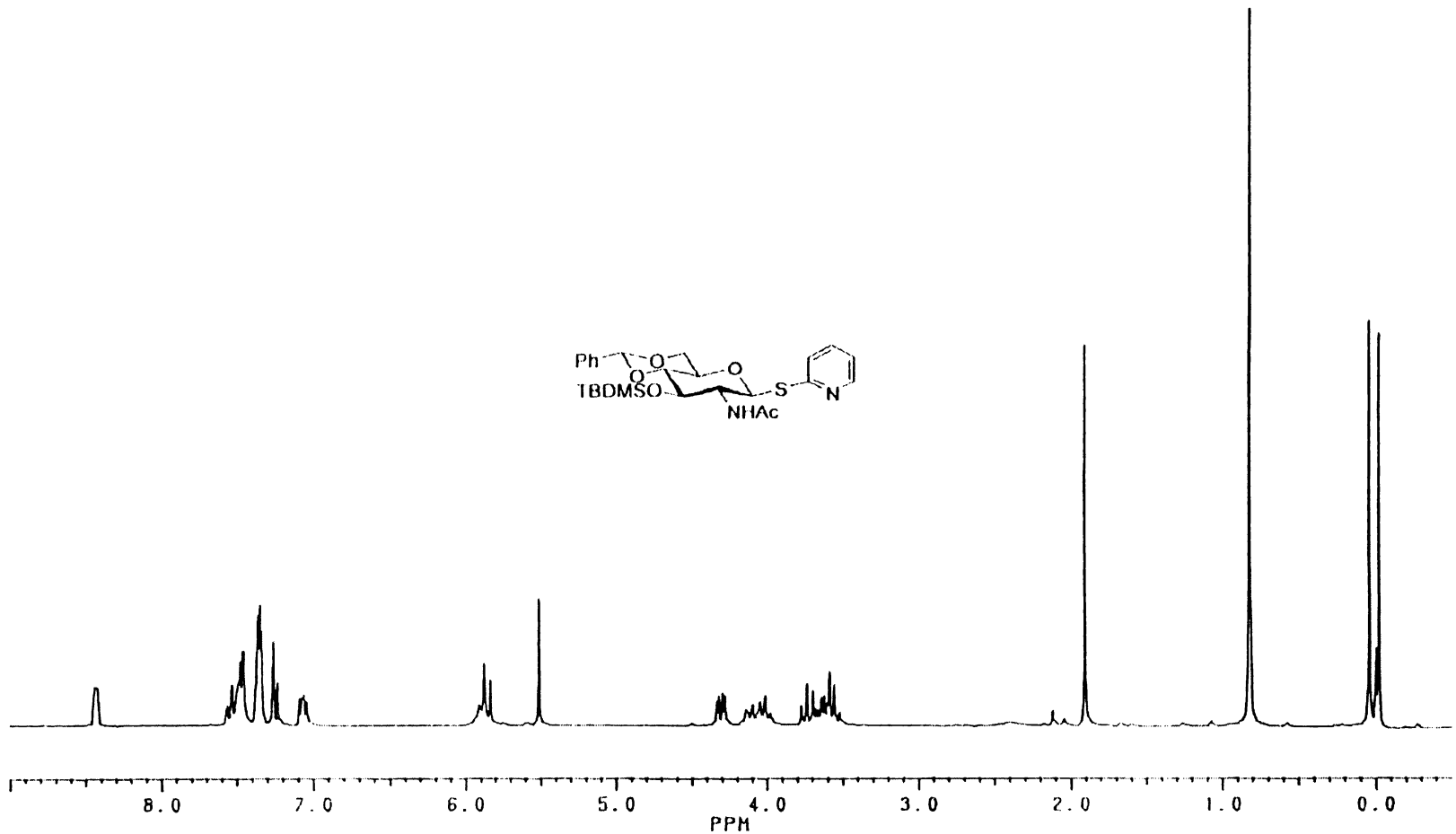
APPENDIX II. NMR SPECTRA (1D AND 2D) OF SELECTED COMPOUNDS



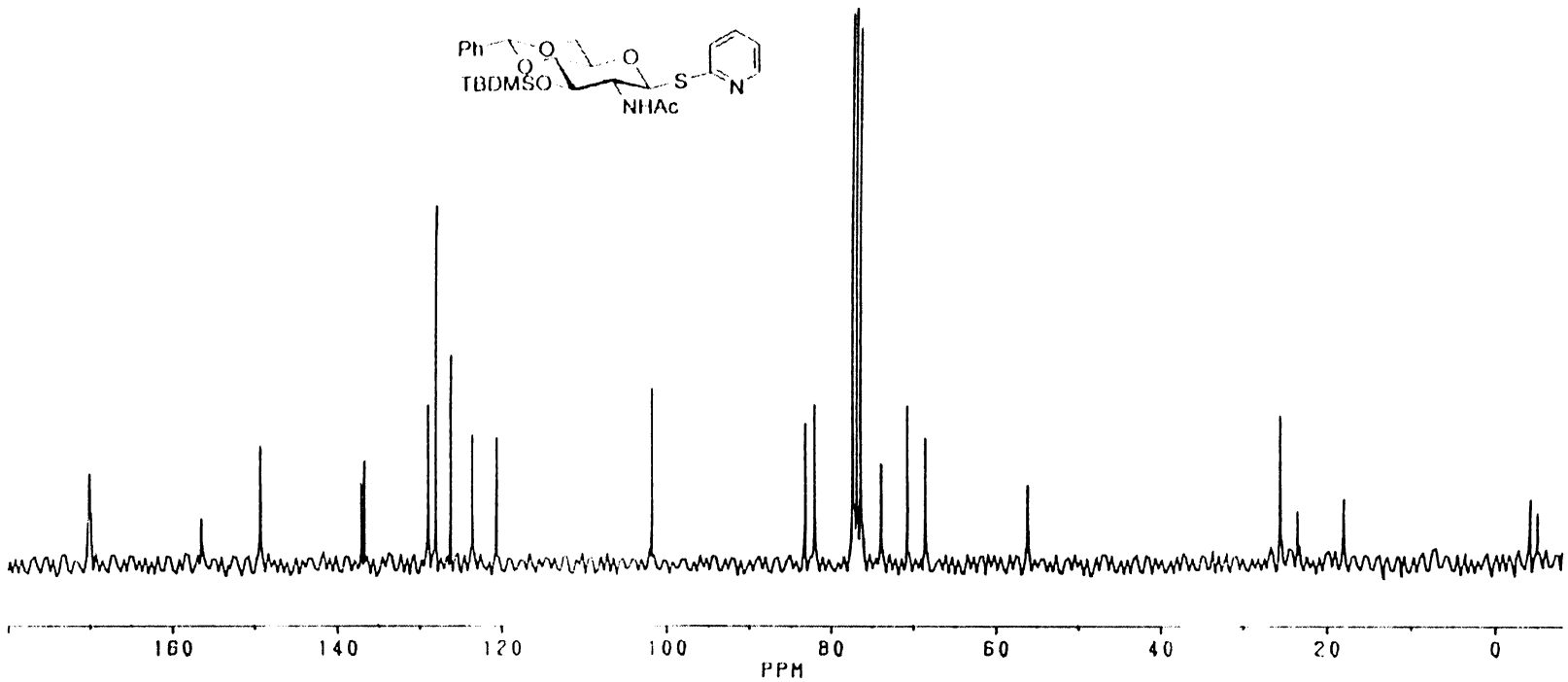
^{1}H NMR spectrum (250 MHz, DMSO-d_6) of 2-pyridinyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (**78**).



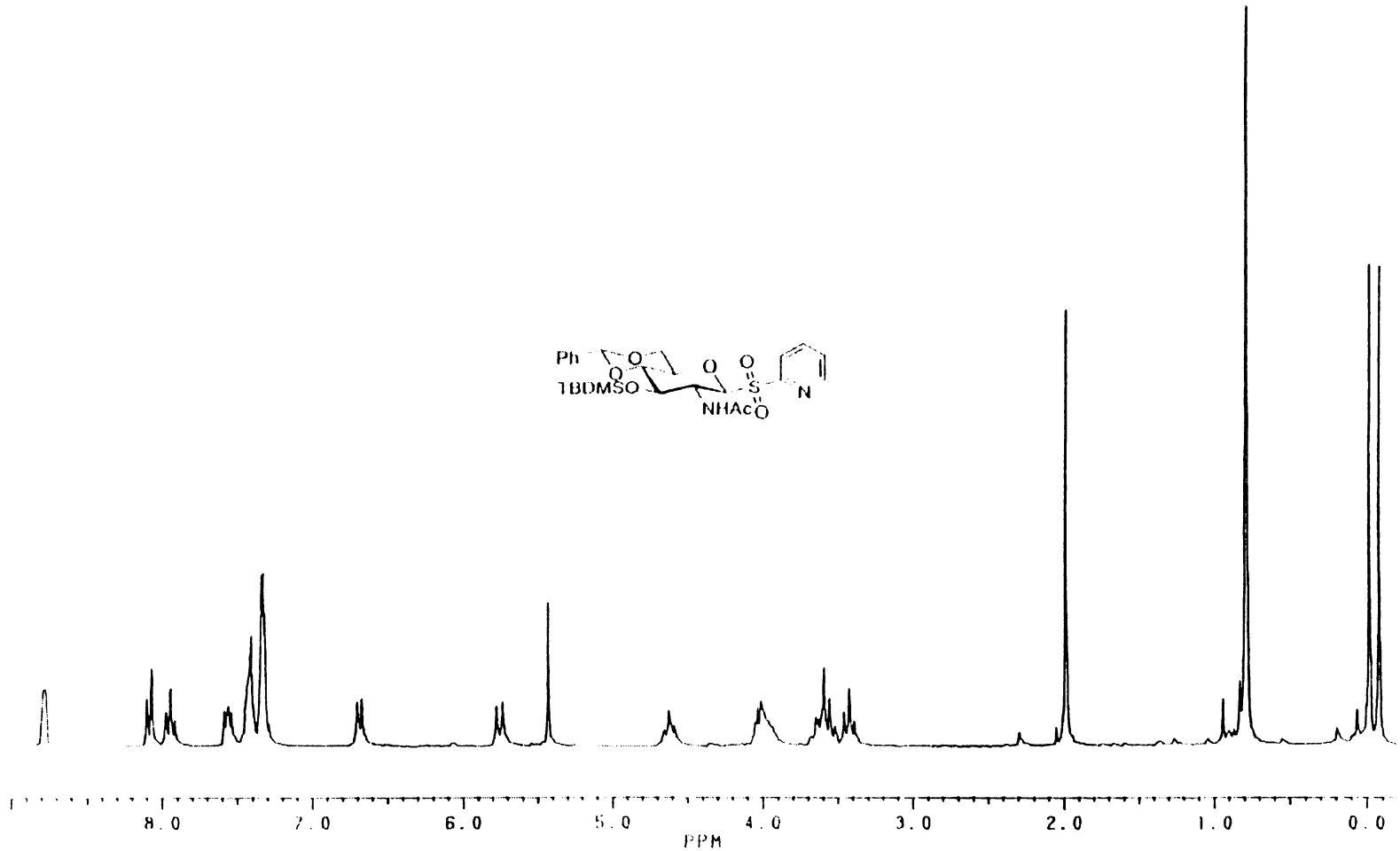
^{13}C NMR spectrum (62.5 MHz, DMSO-d_6) of 2-pyridinyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (**78**).



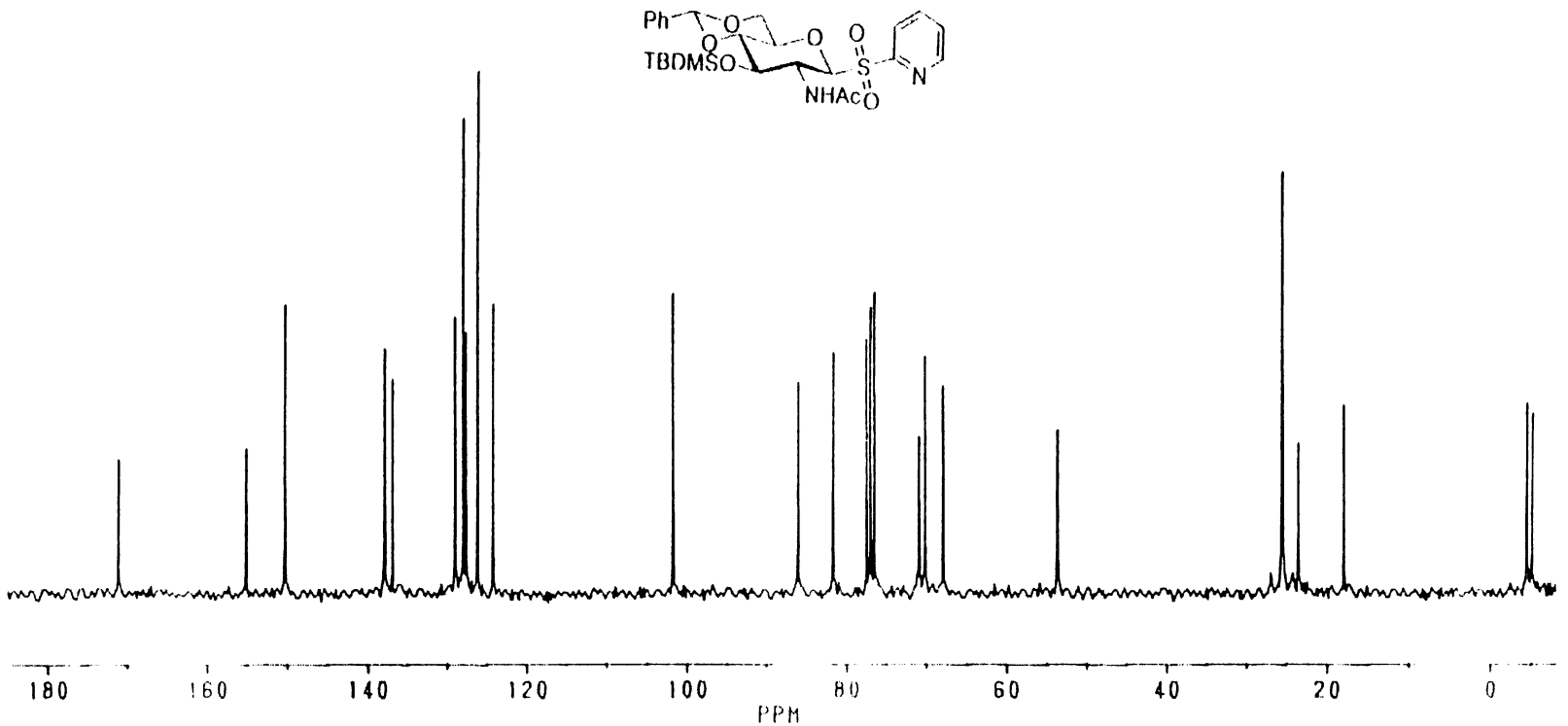
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of 2-pyridinyl 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-1-thio-β-D-glucopyranoside (**79**).



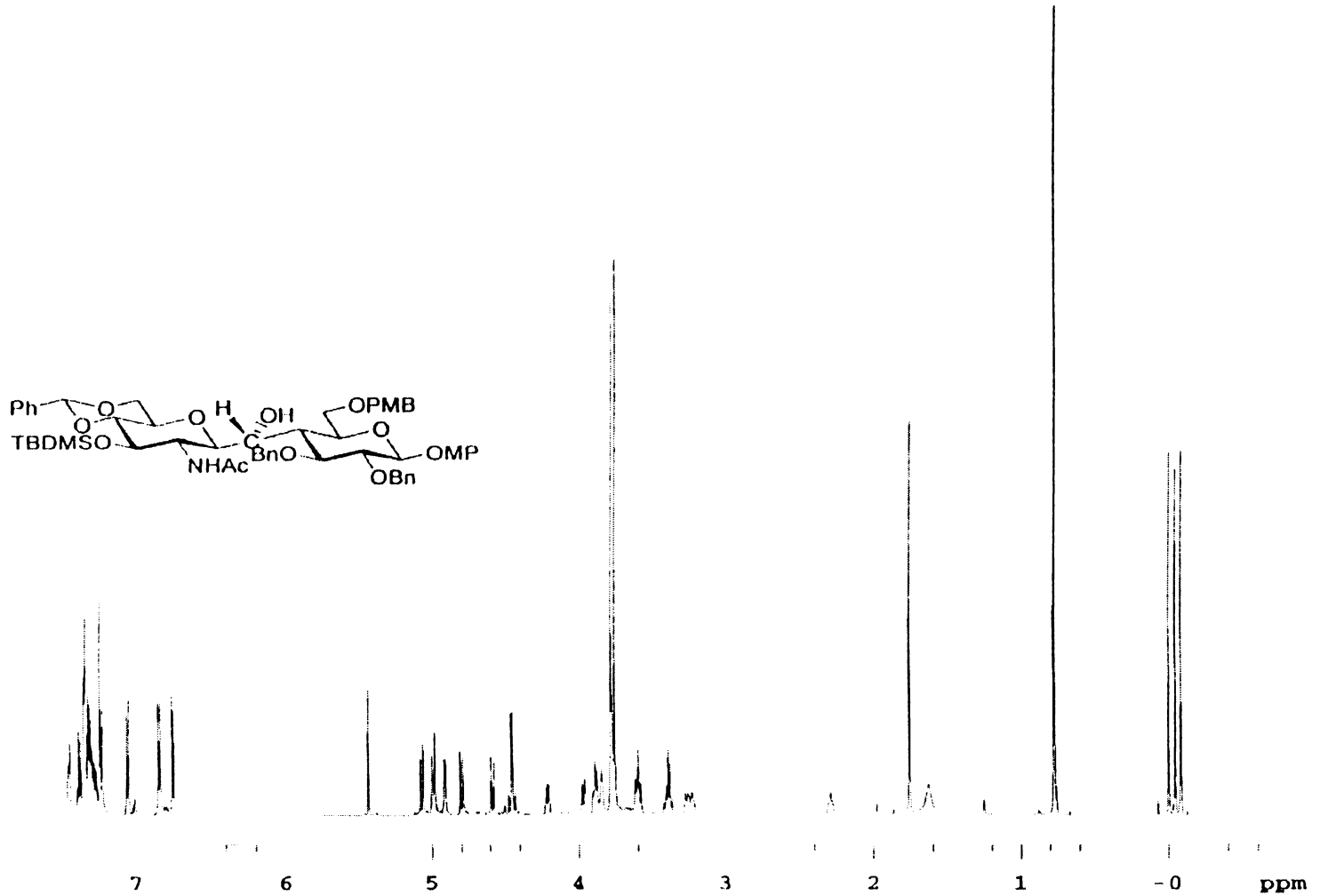
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of 2-pyridinyl 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-1-thio-*β*-D-glucopyranoside (**79**).



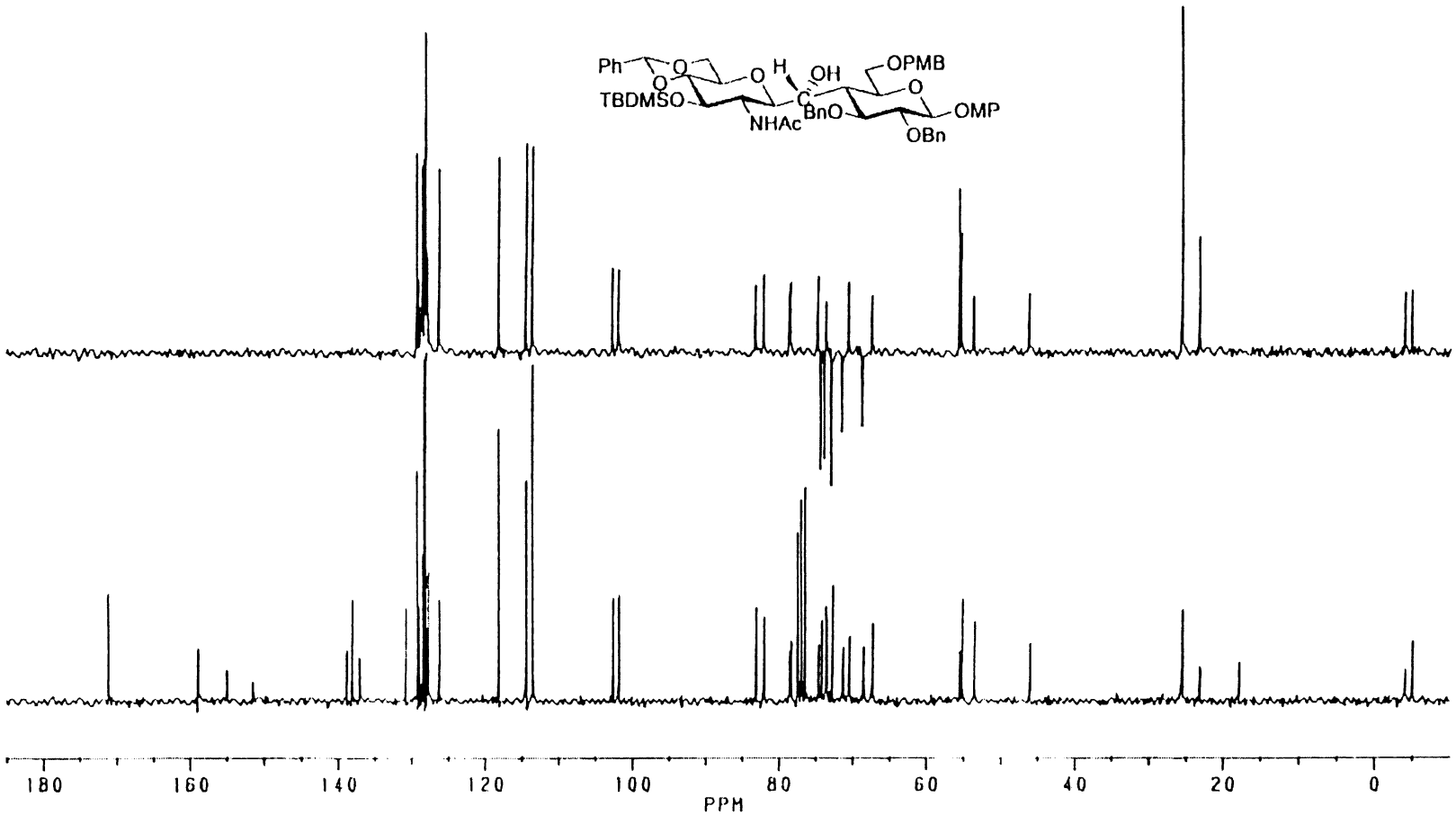
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose (**20**).



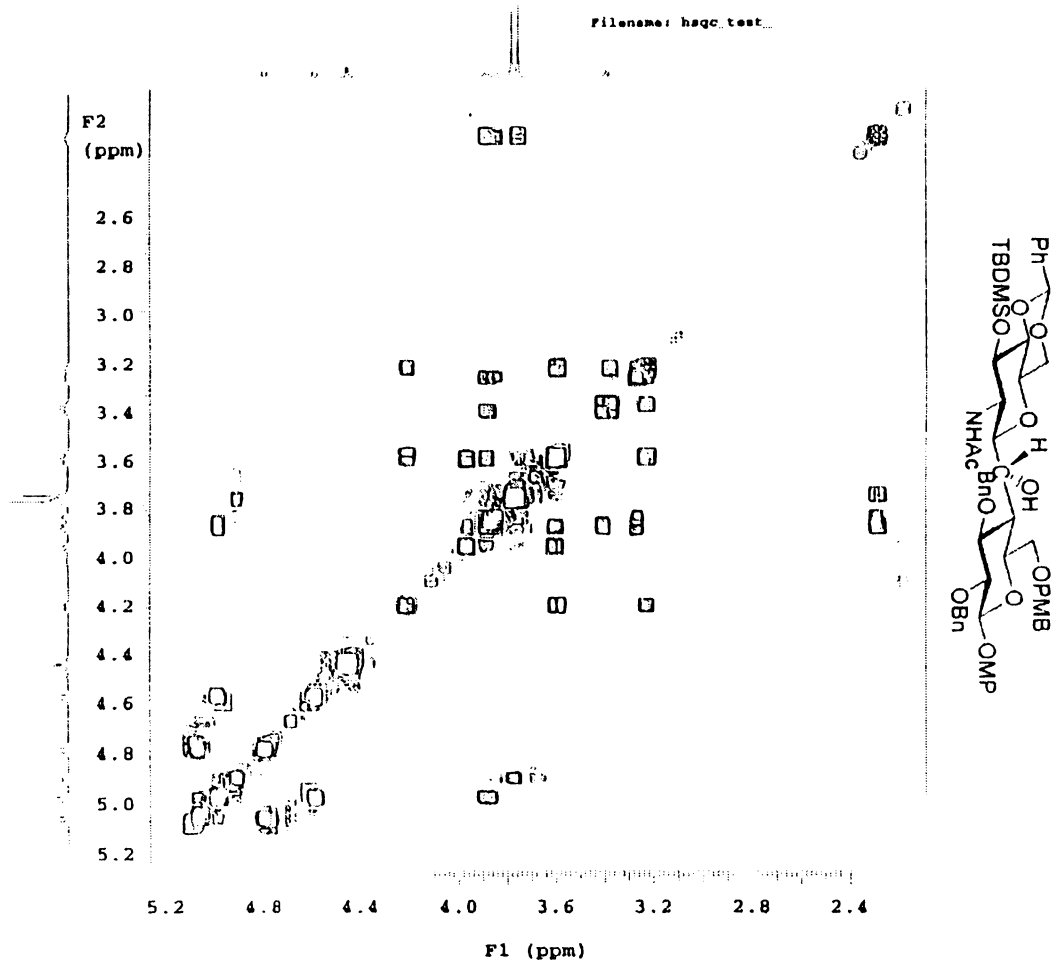
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of 2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1,2-dideoxy-1-pyridinylsulfonyl-β-D-glucopyranose (**20**).



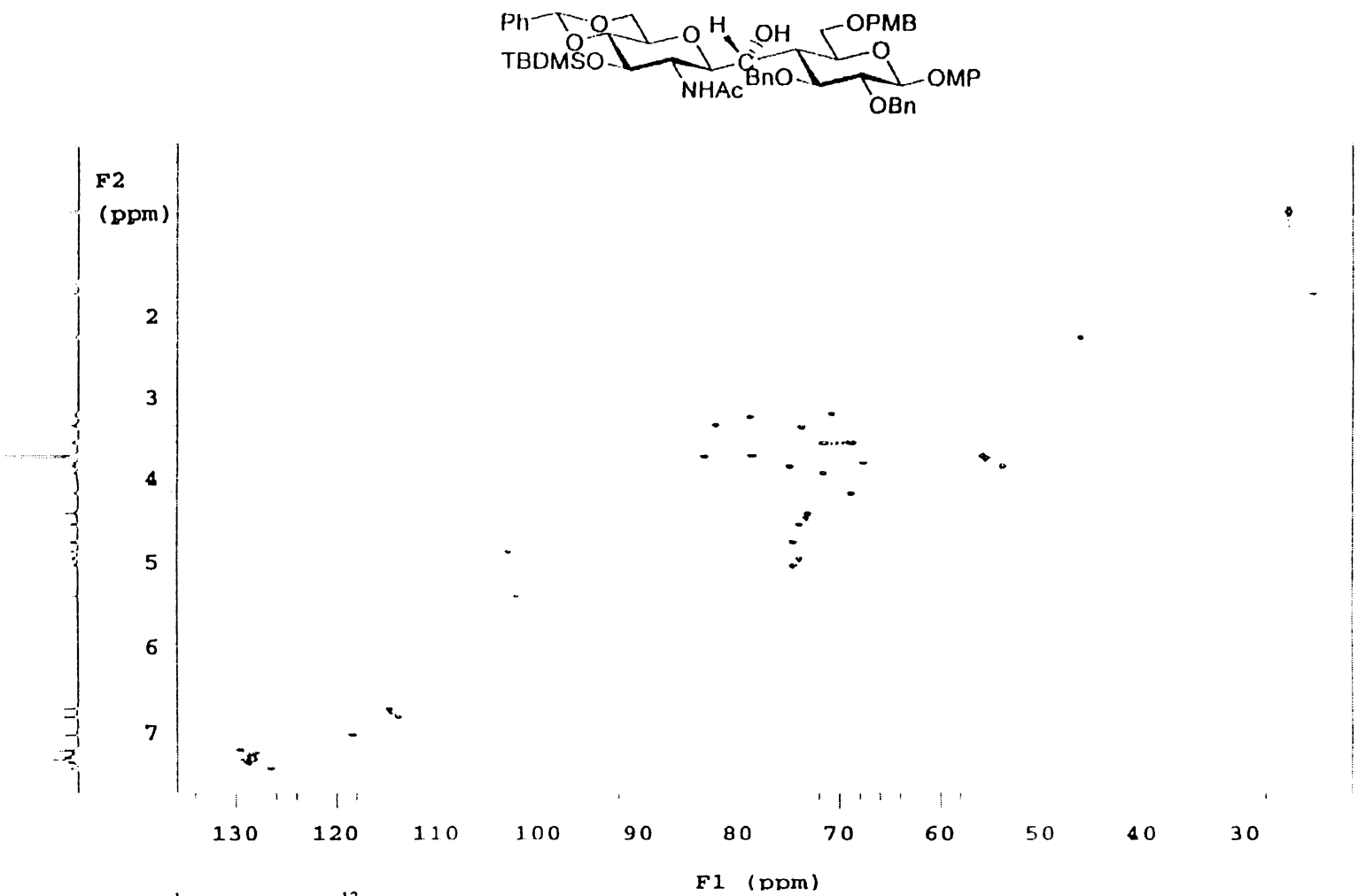
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80a**).



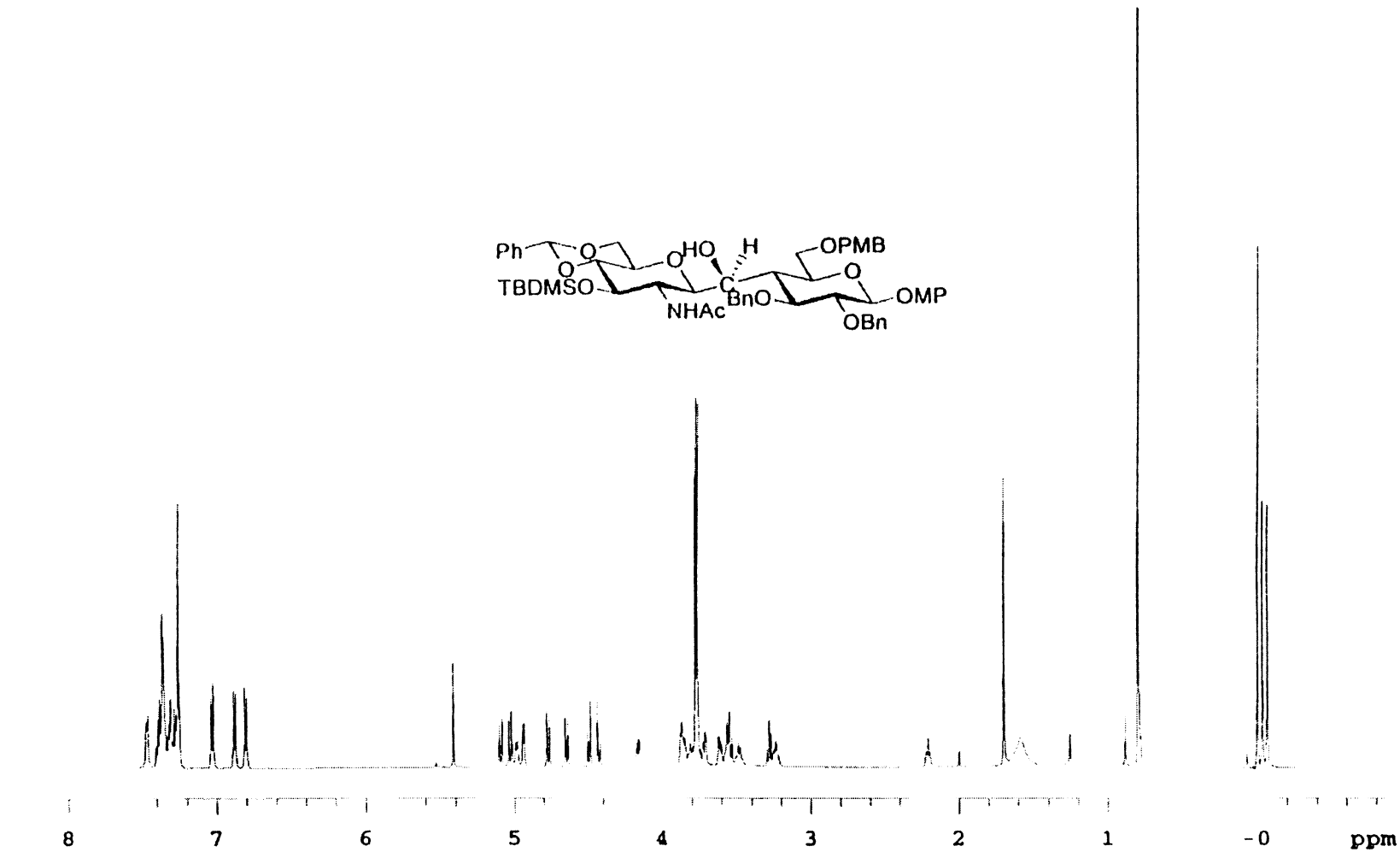
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80a**).



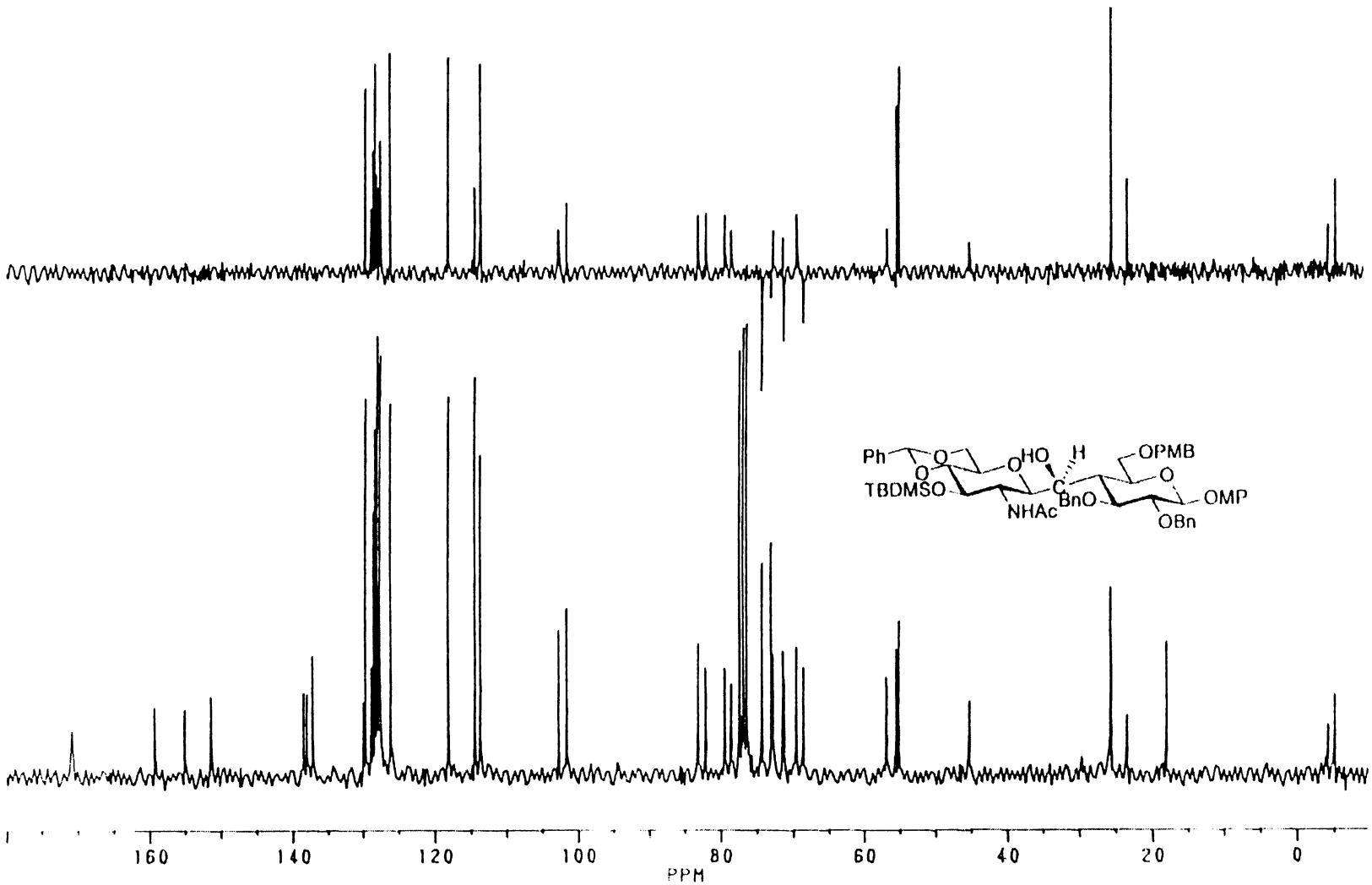
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80a**).



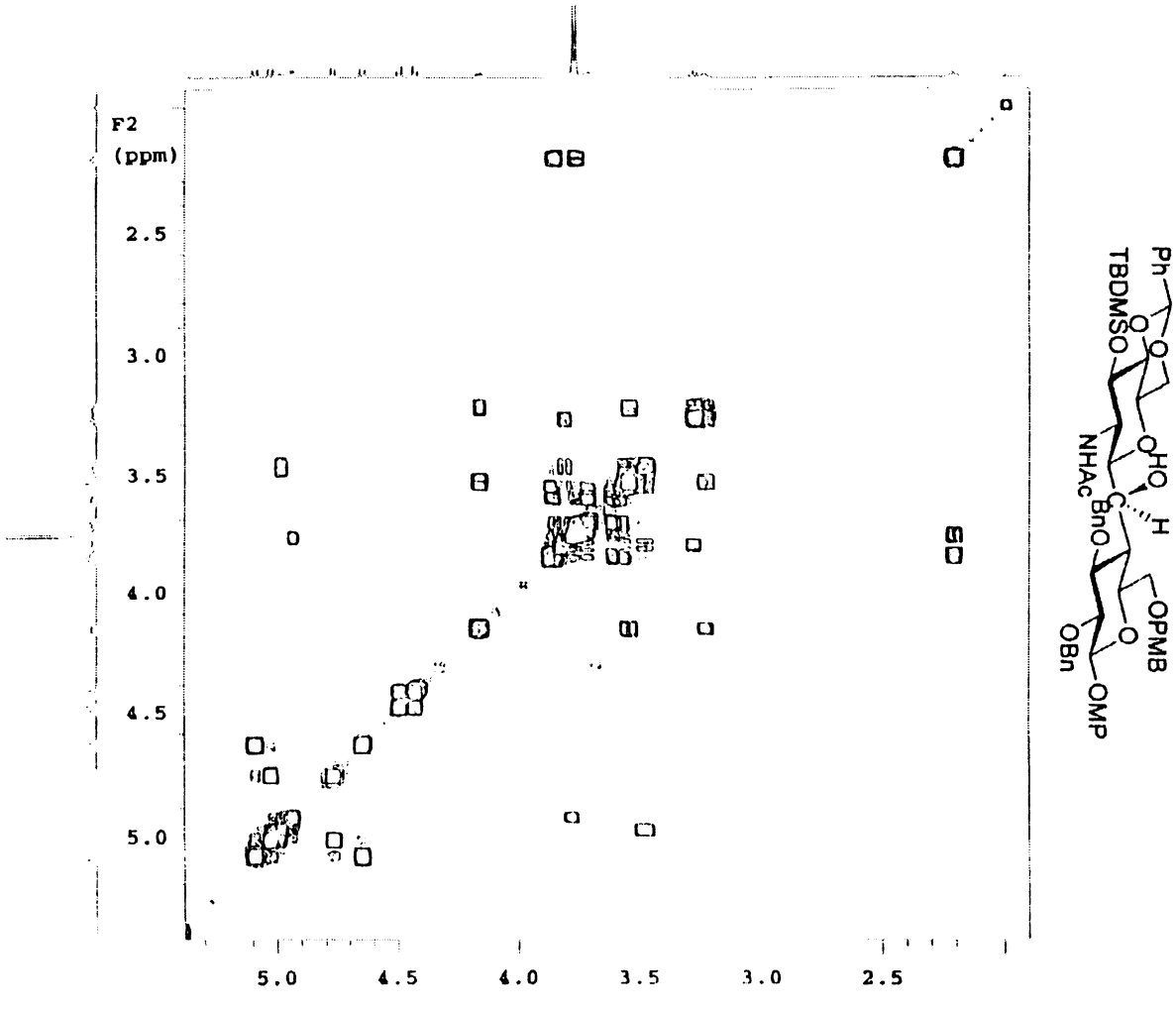
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80a**).



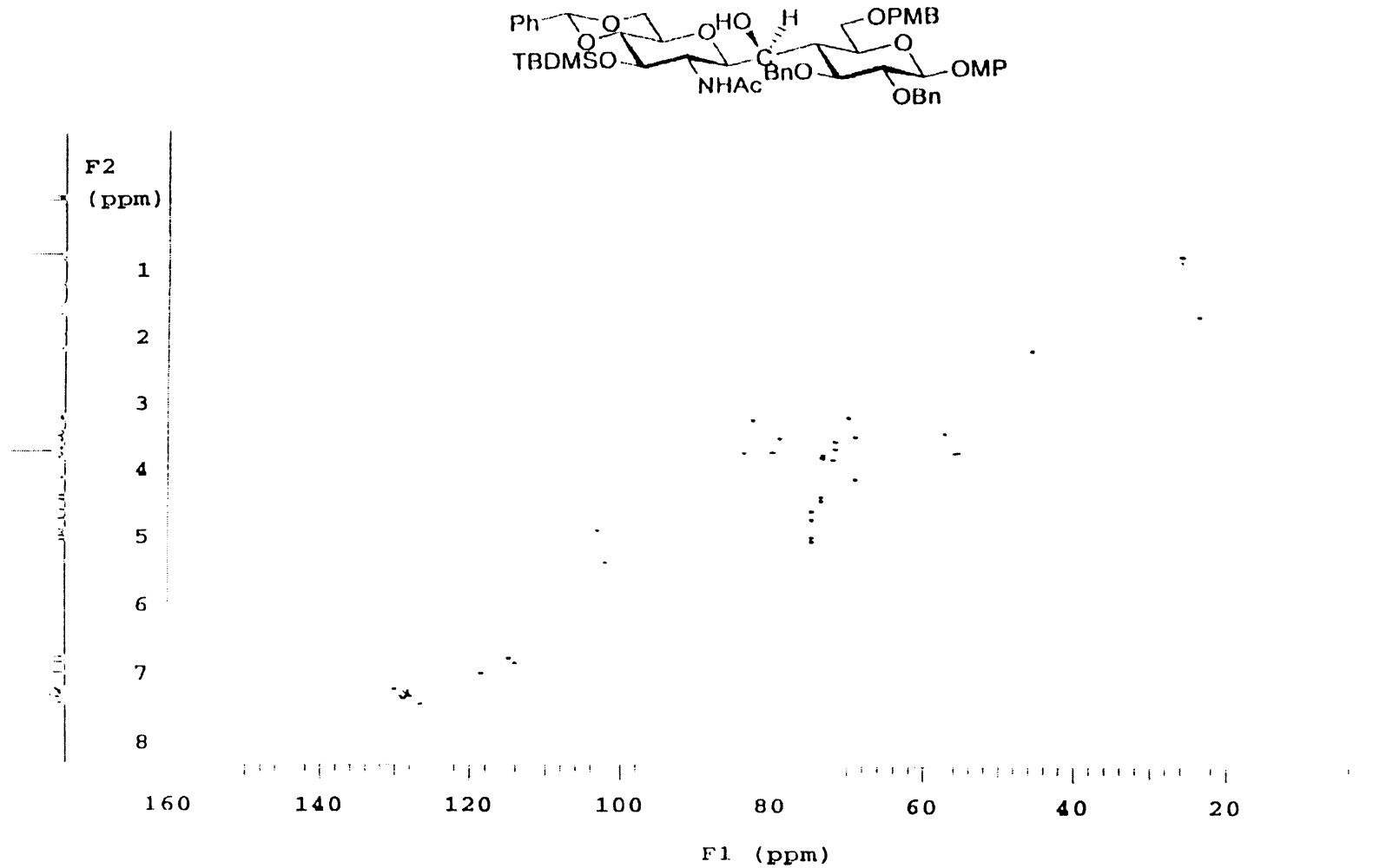
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80b**).



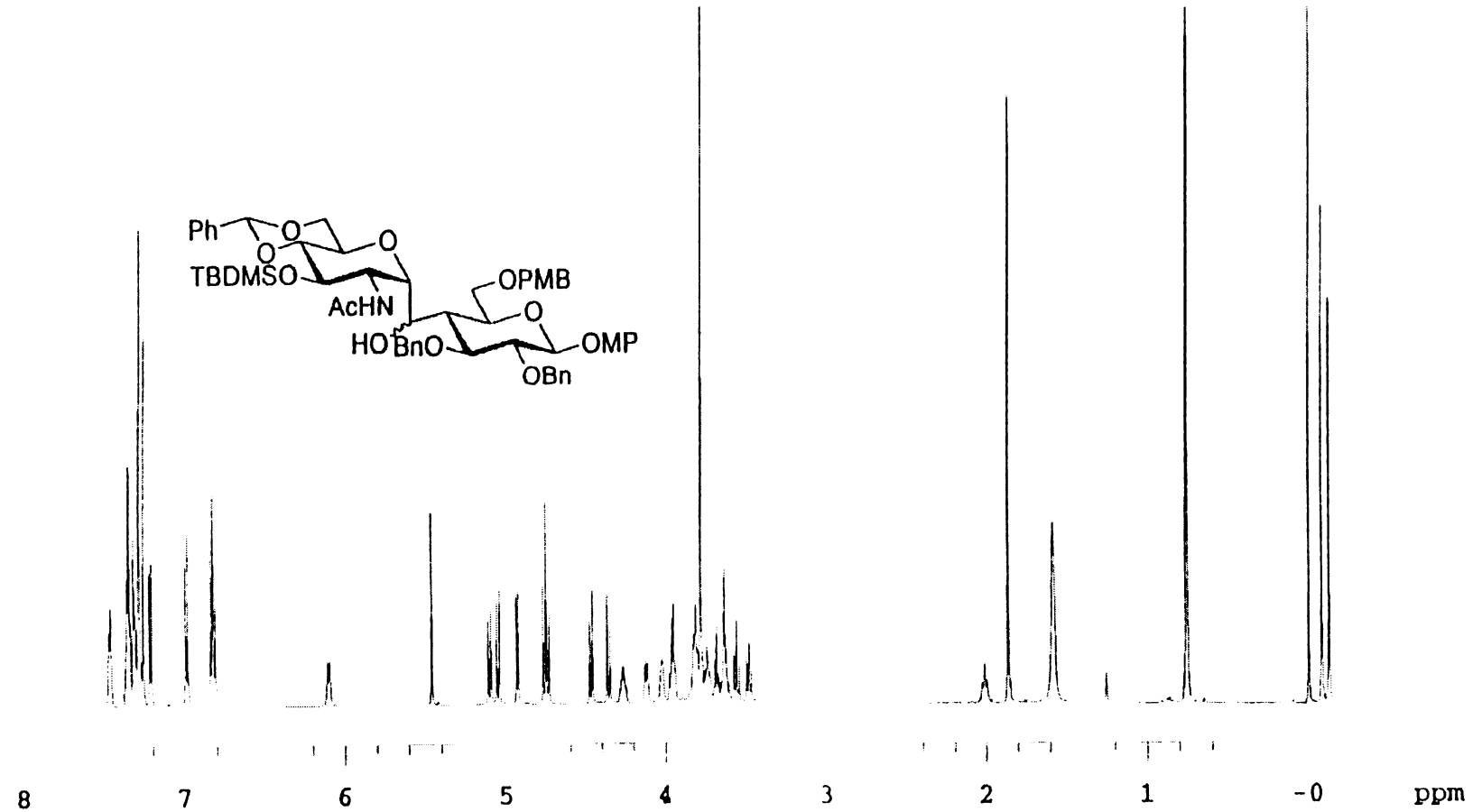
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80b**).



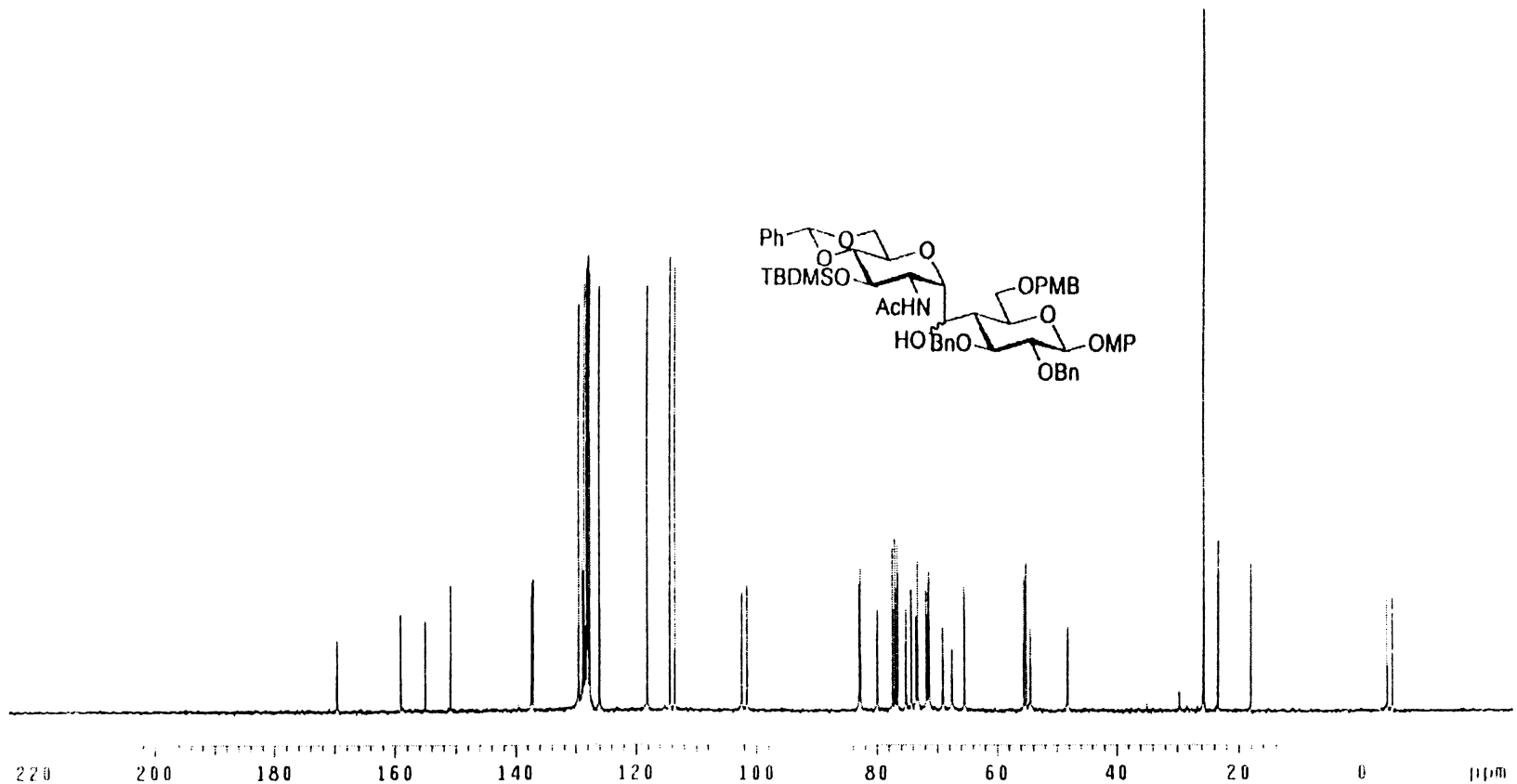
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80b**).



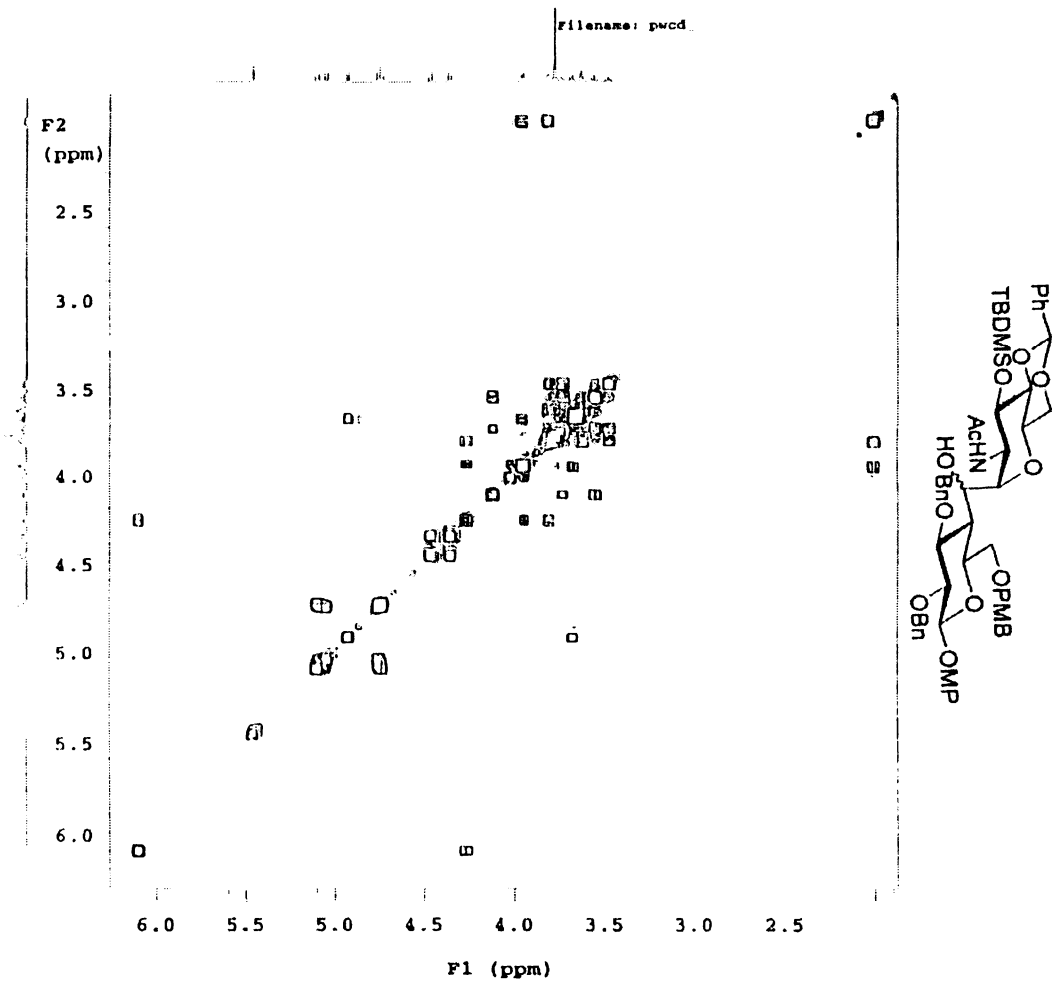
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**80b**).



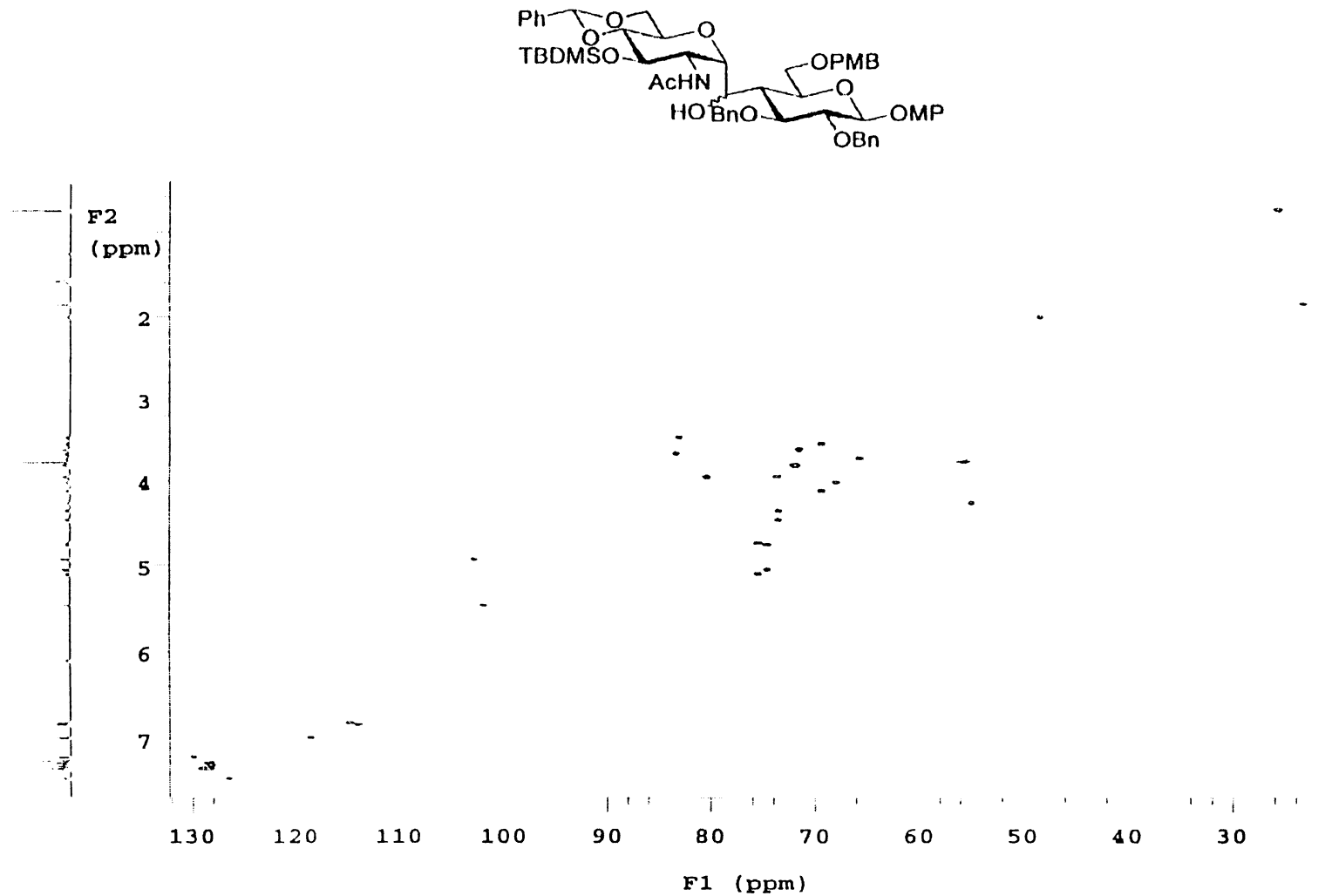
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-α-D-glucopyranoside (**80c**).



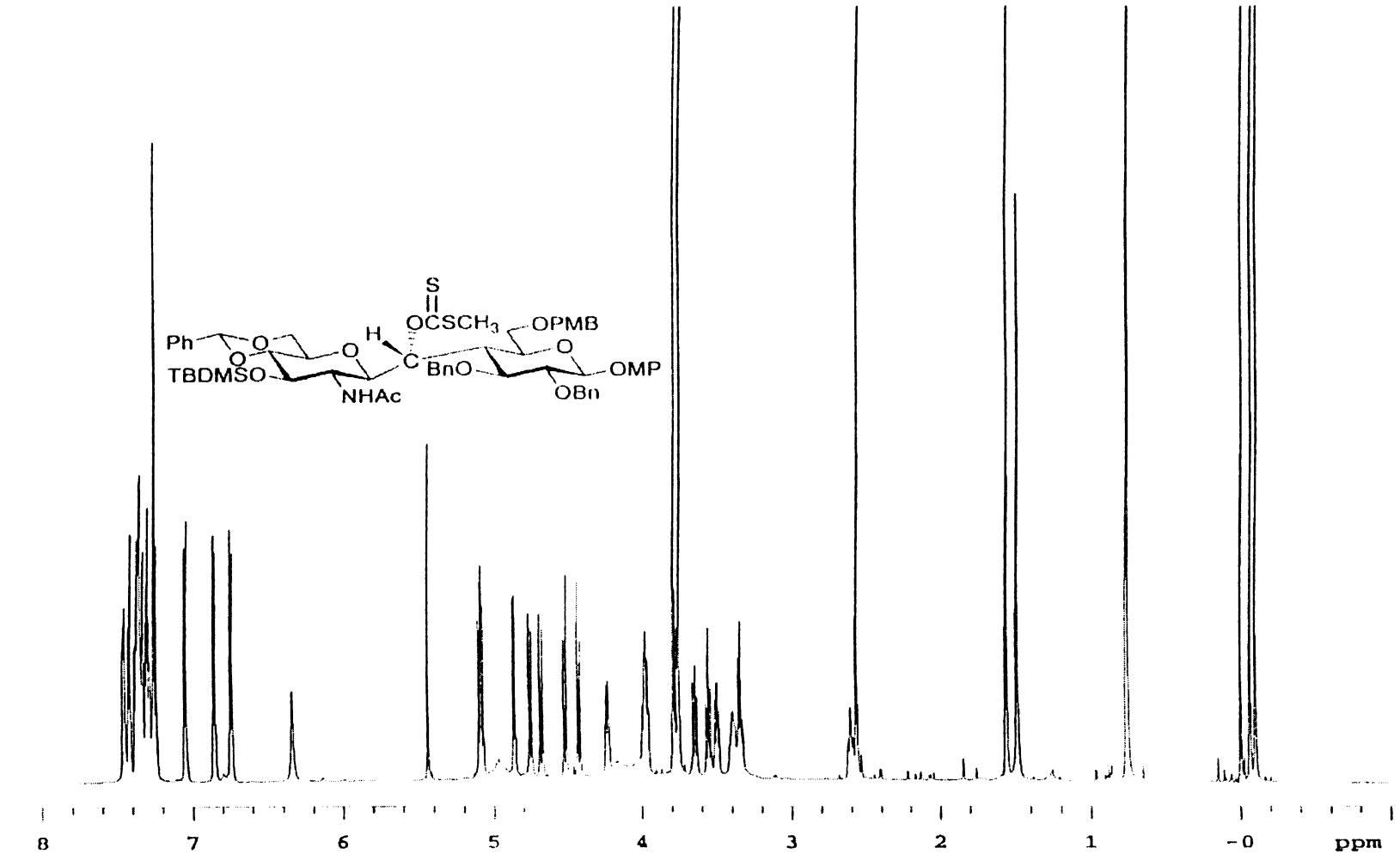
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-α-D-glucopyranoside (**80c**).



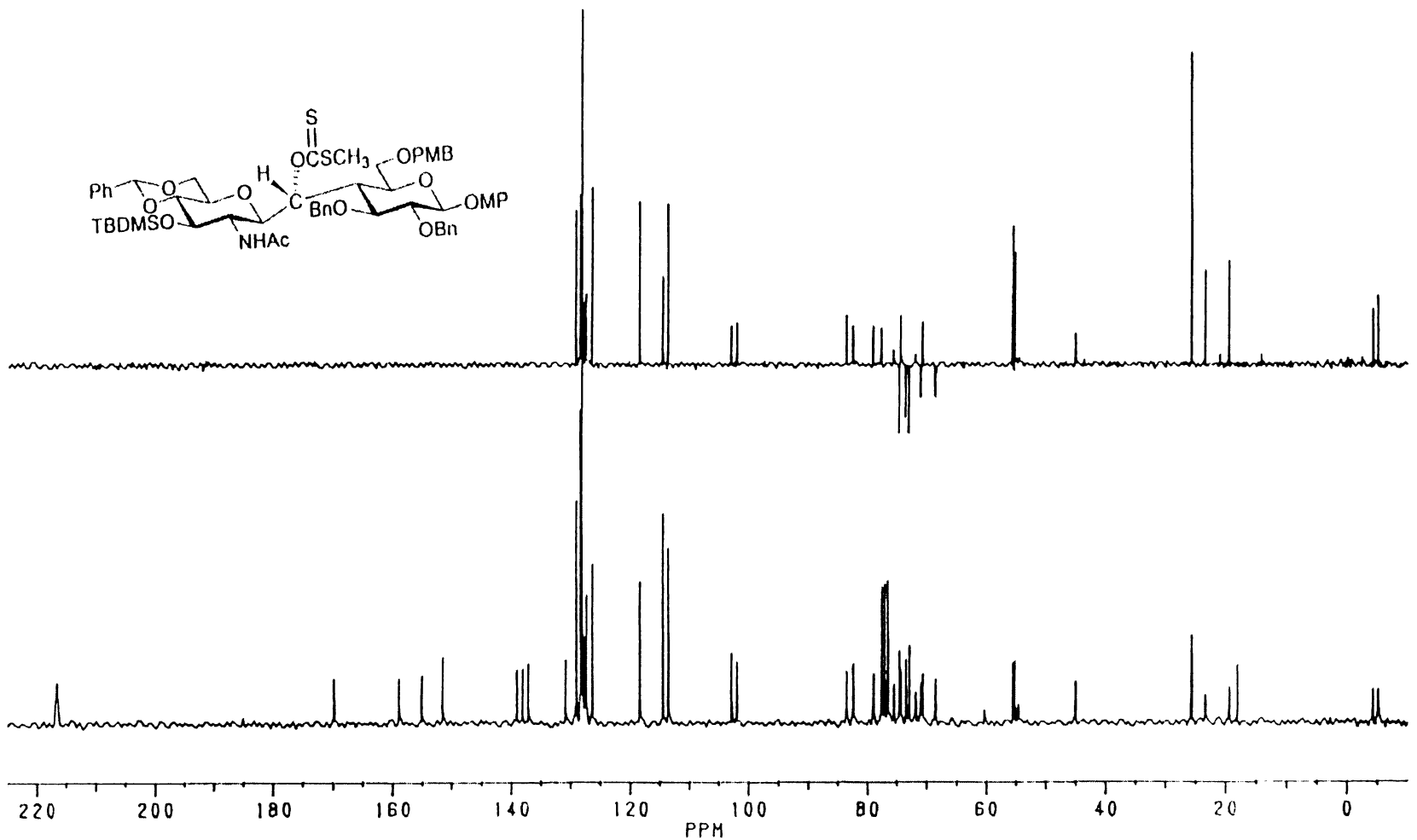
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-α-D-glucopyranoside (**80c**).



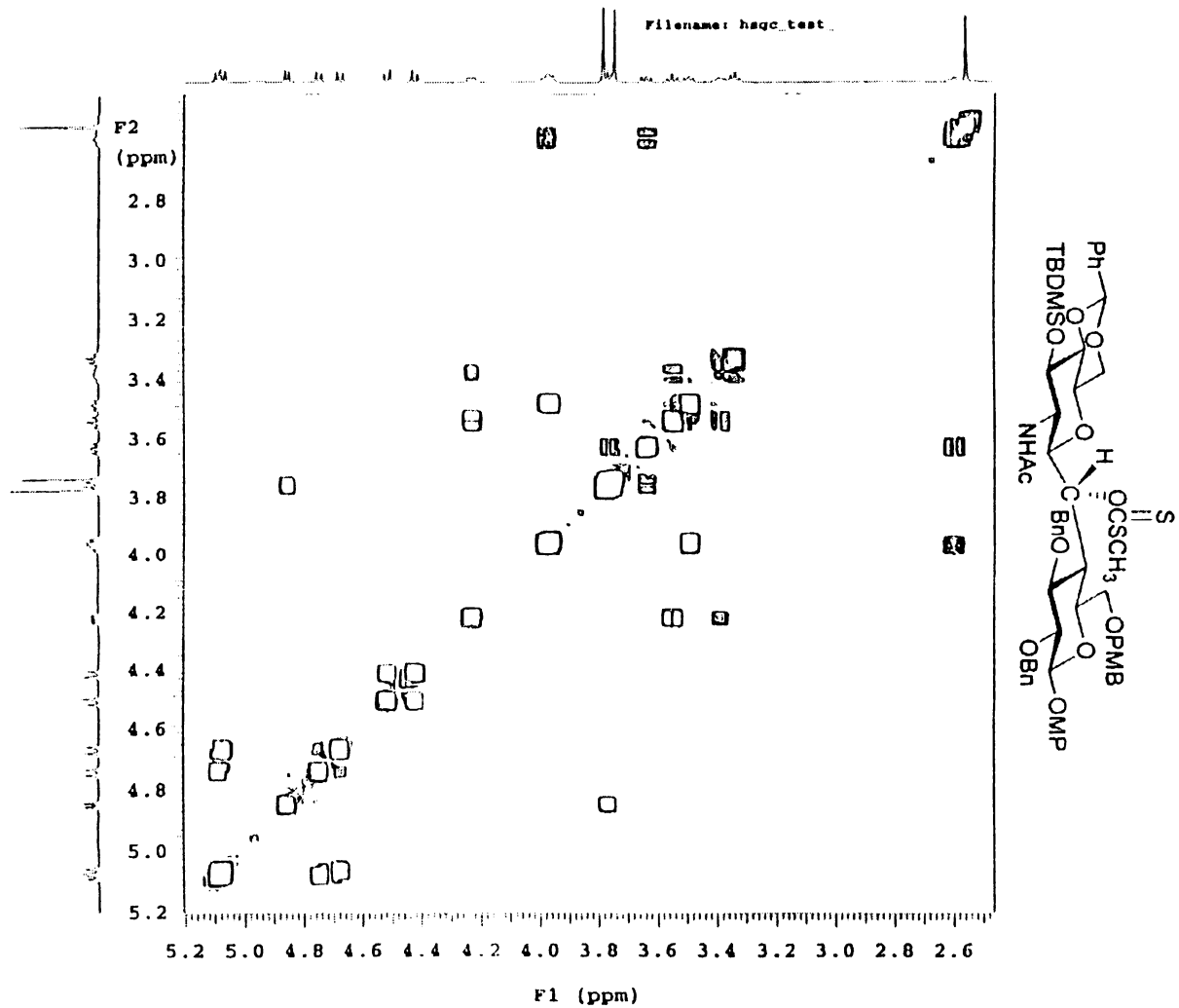
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-4a-hydroxy-6-*O*-*p*-methoxybenzyl-4a-carba-α-D-glucopyranoside (**80c**).



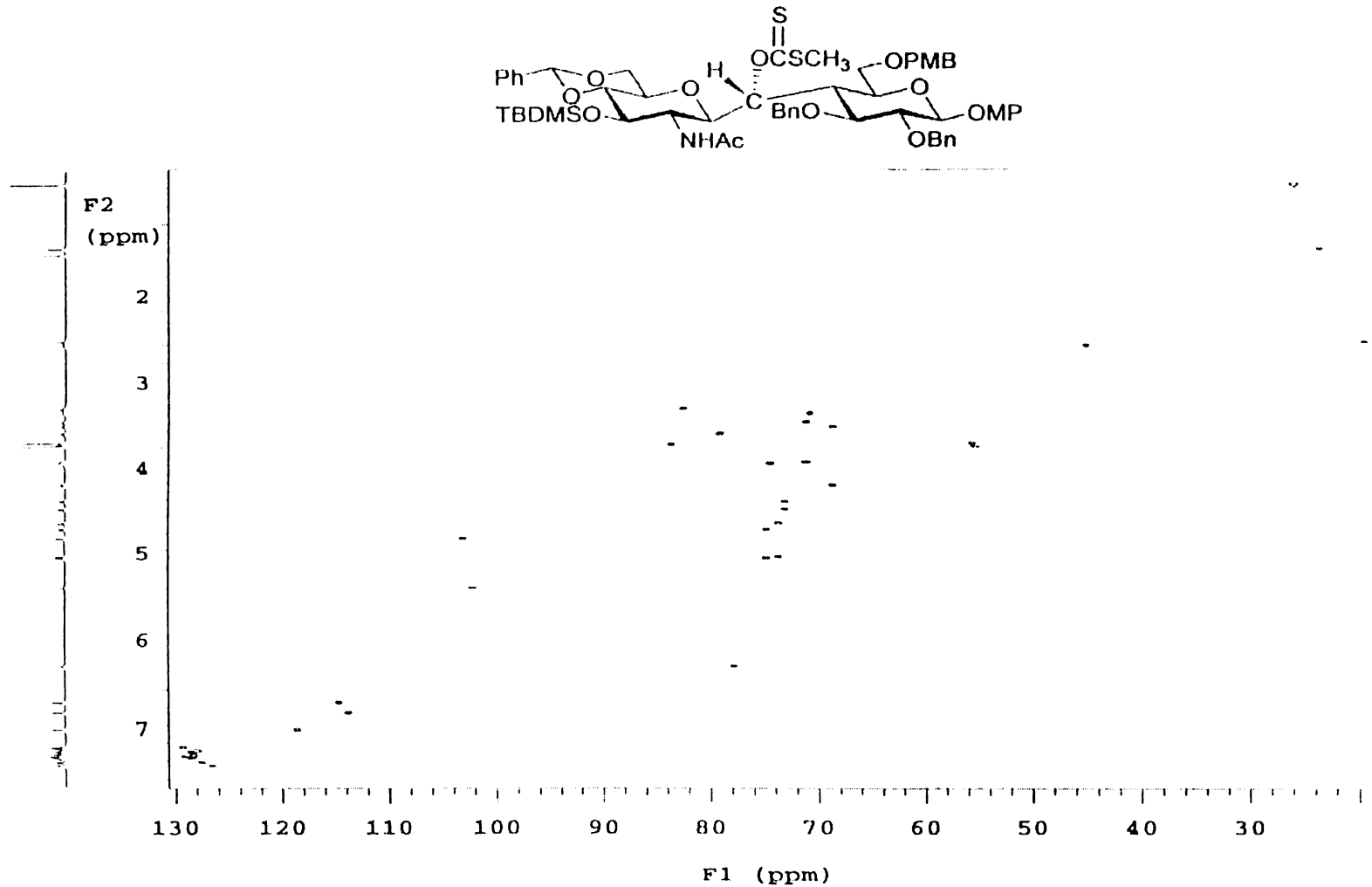
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (**83a**).



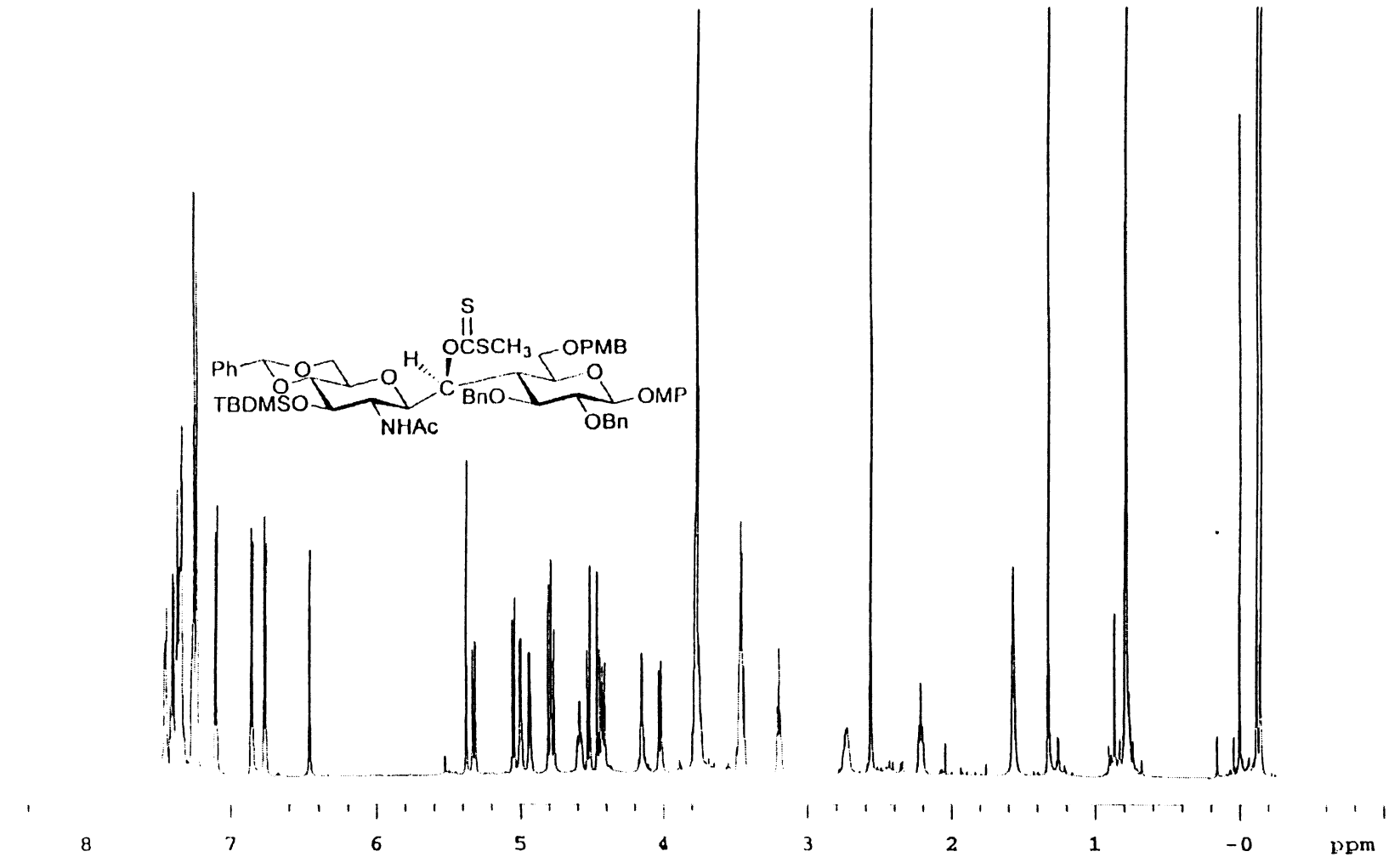
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (**83a**).



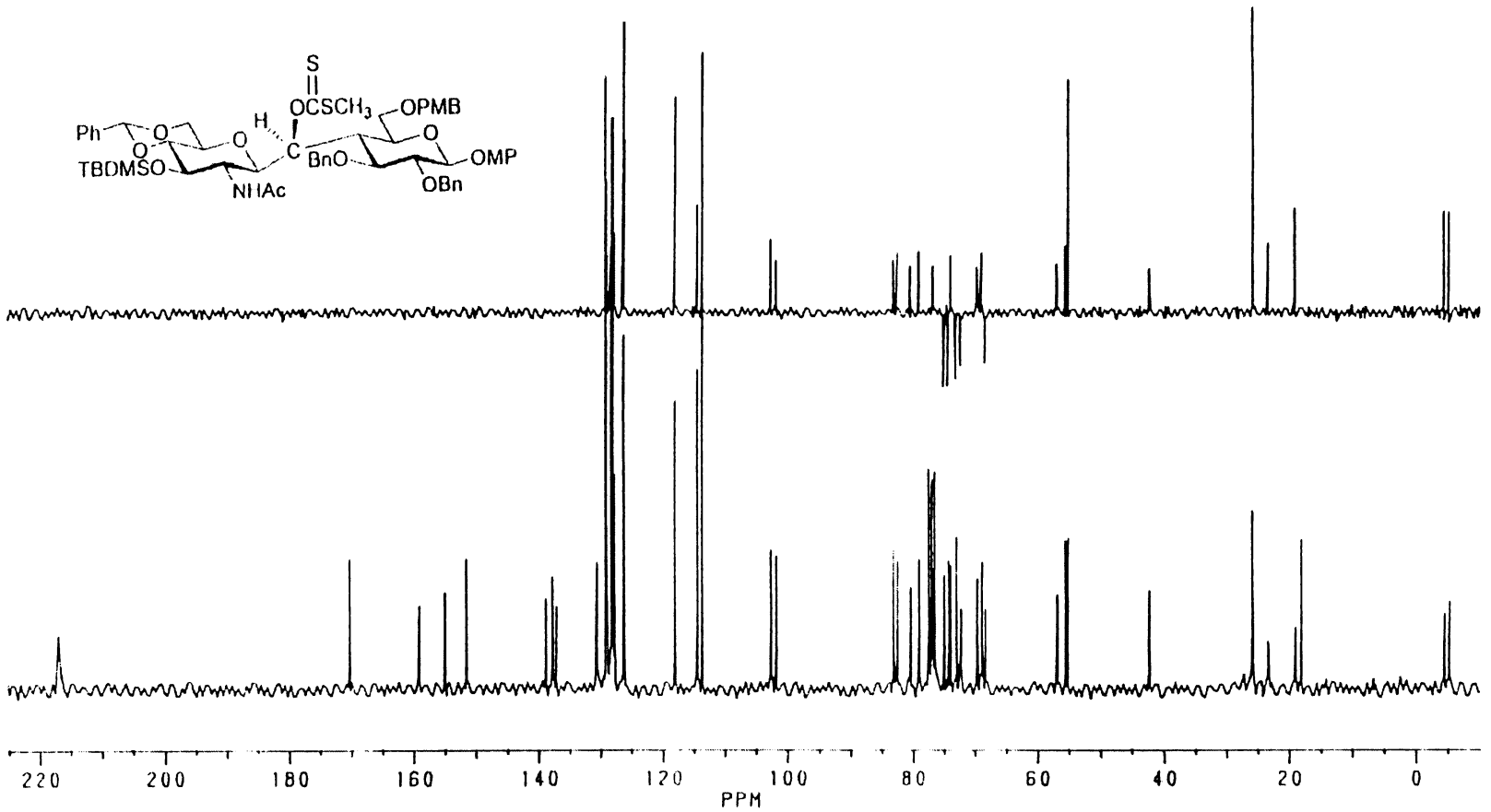
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**83a**).



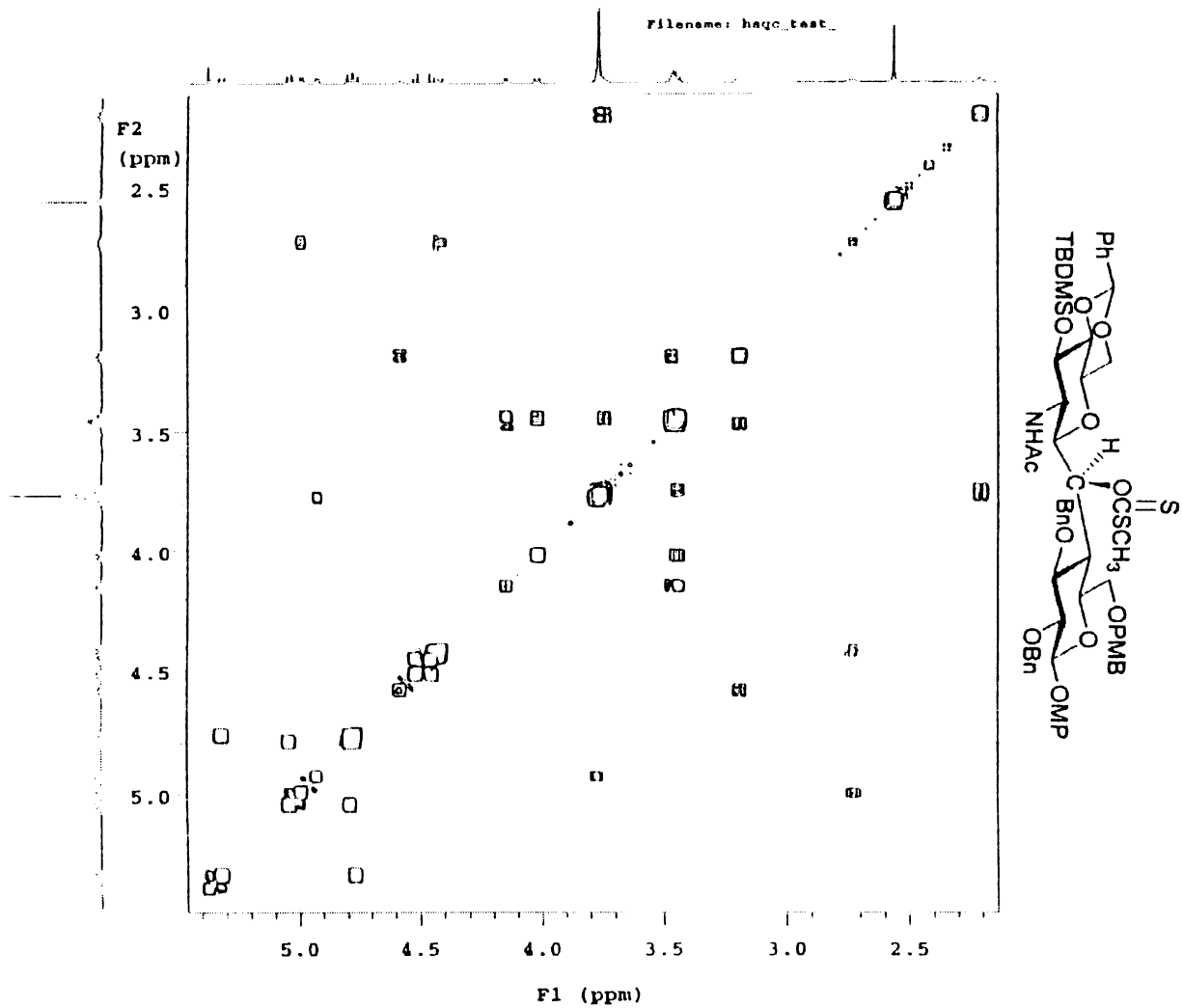
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*R*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**83a**).



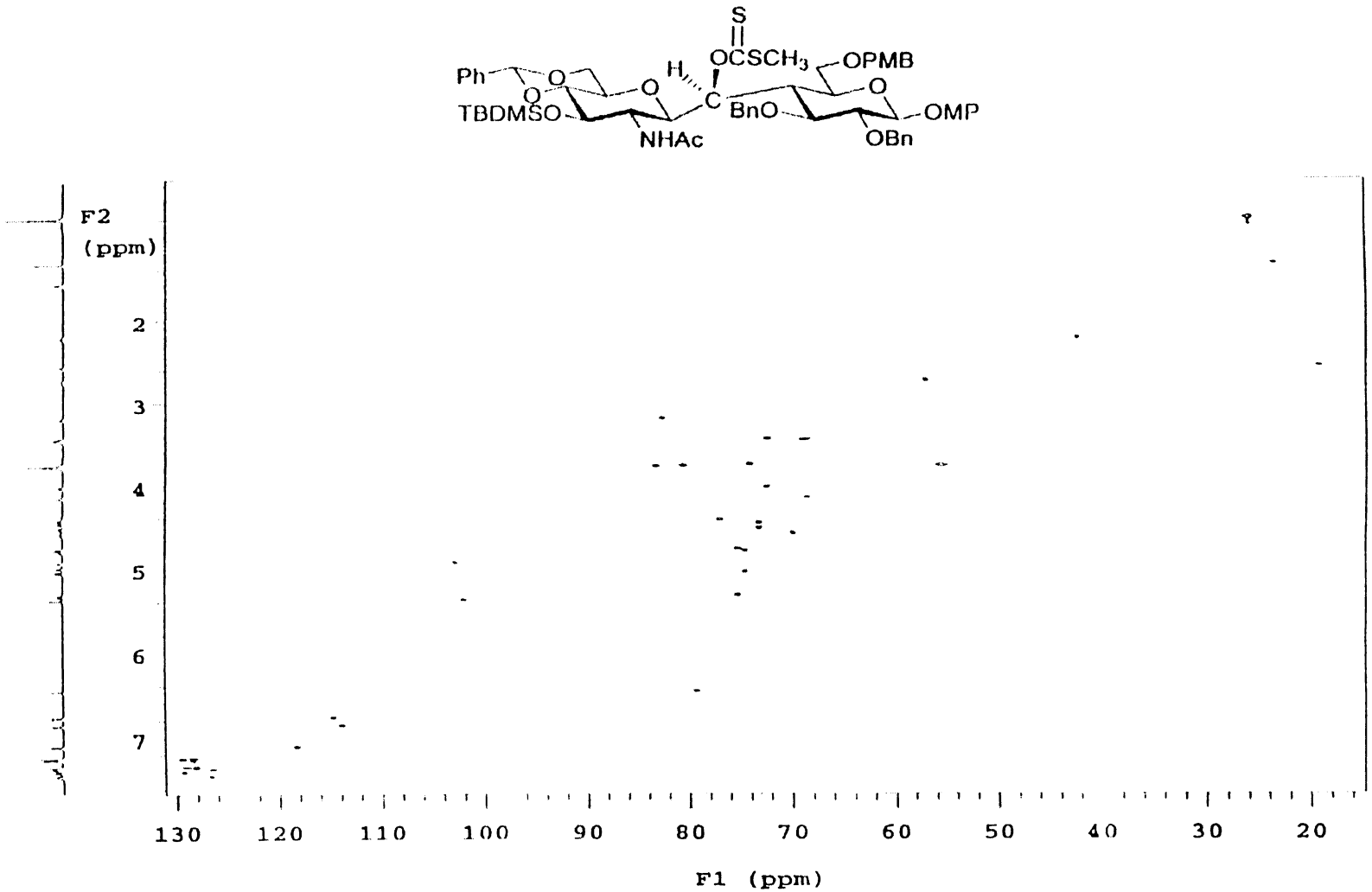
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (**83b**).



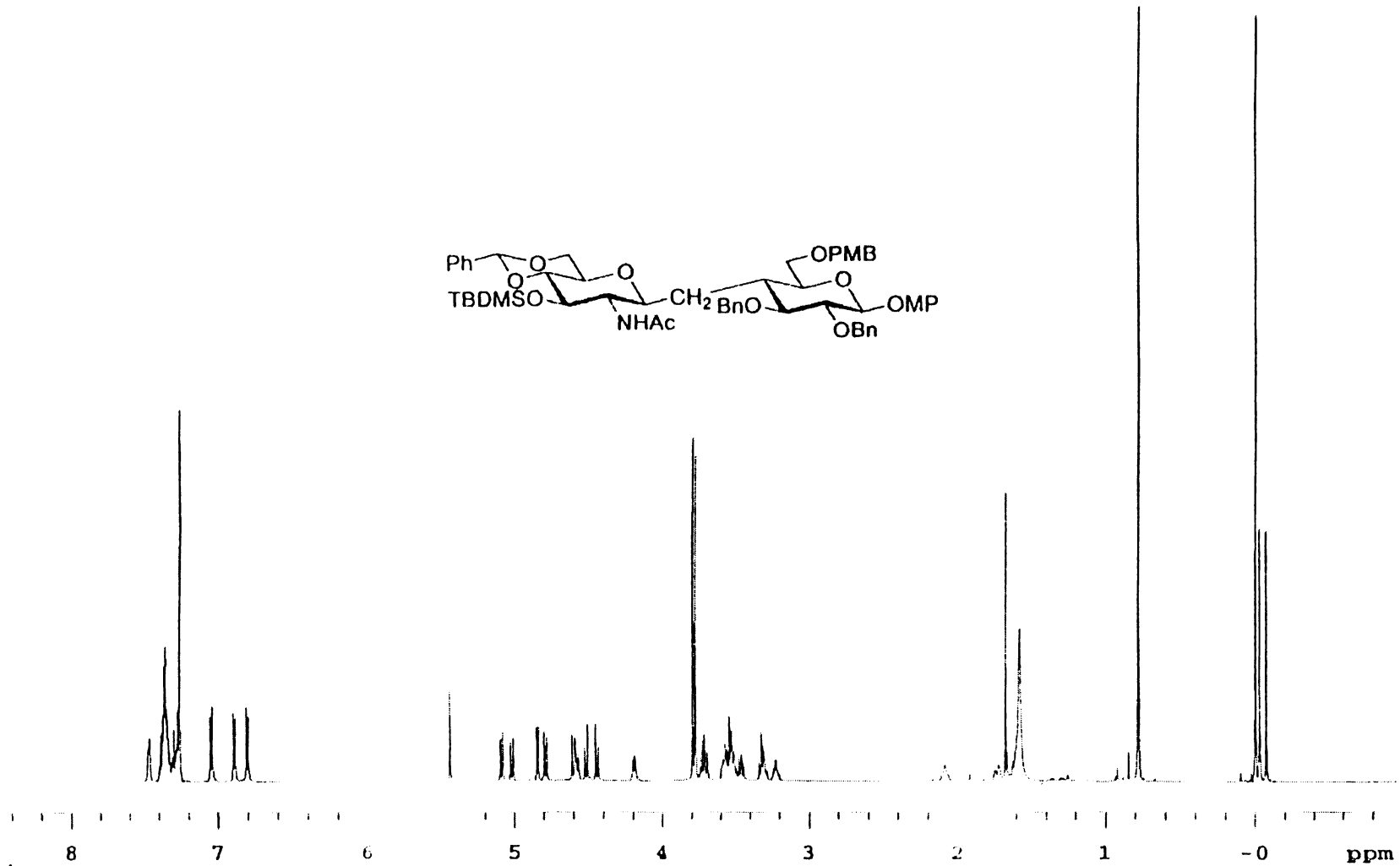
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (**83b**).



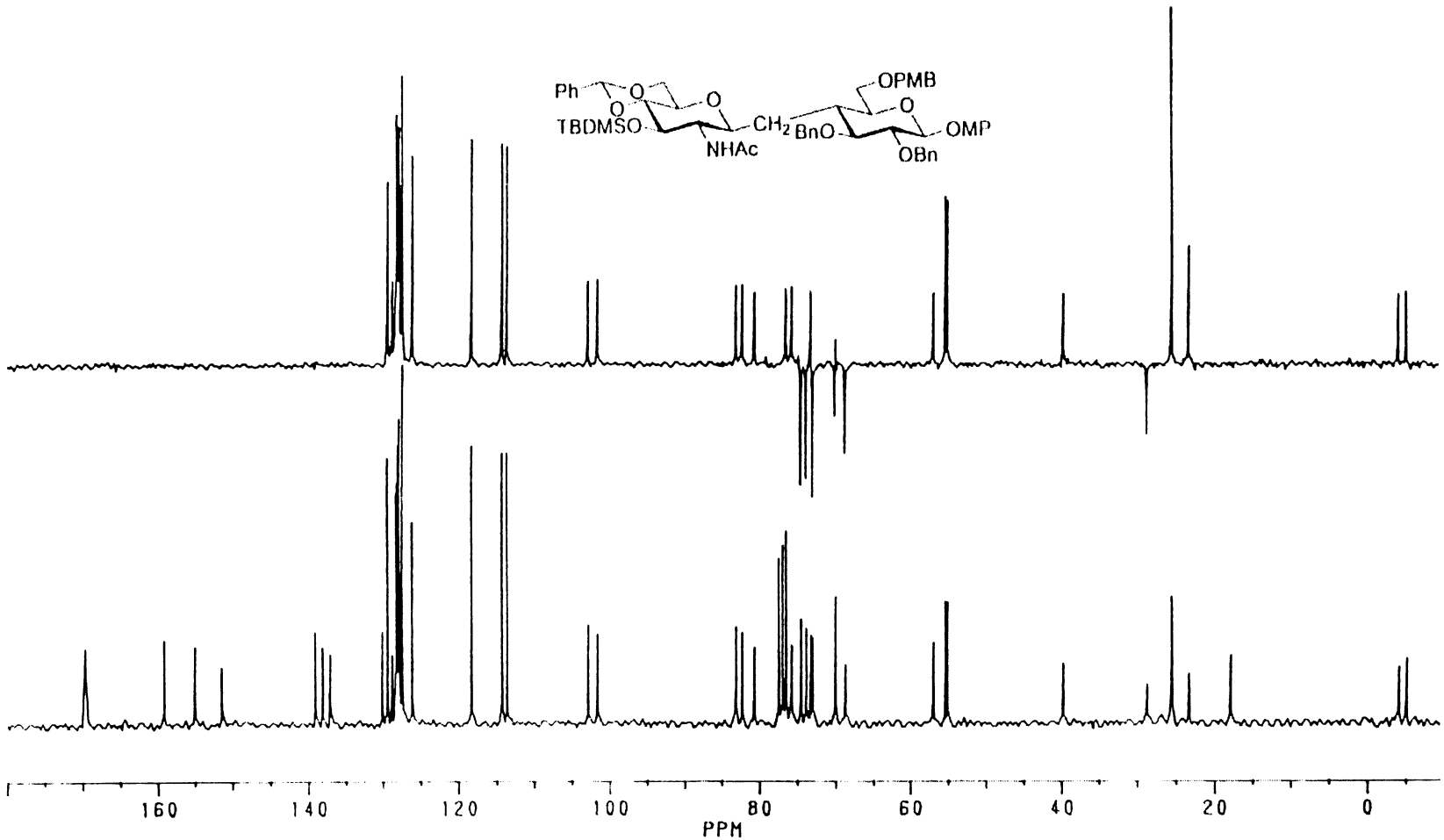
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-*O*-methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**83b**).



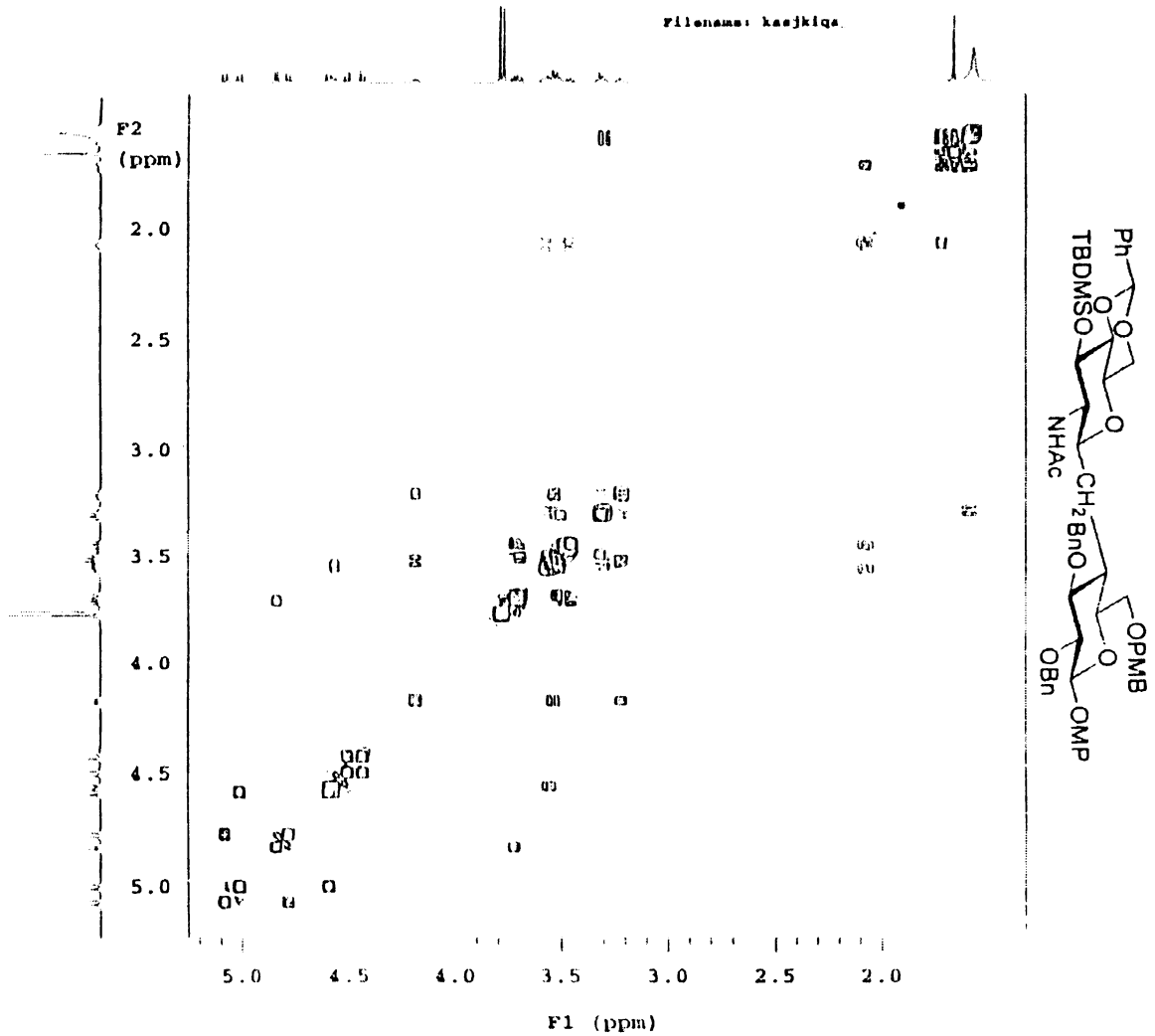
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-(4a*S*)-2,3-di-*O*-benzyl-4a-*O*- methylthiothiocarbonyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**83b**).



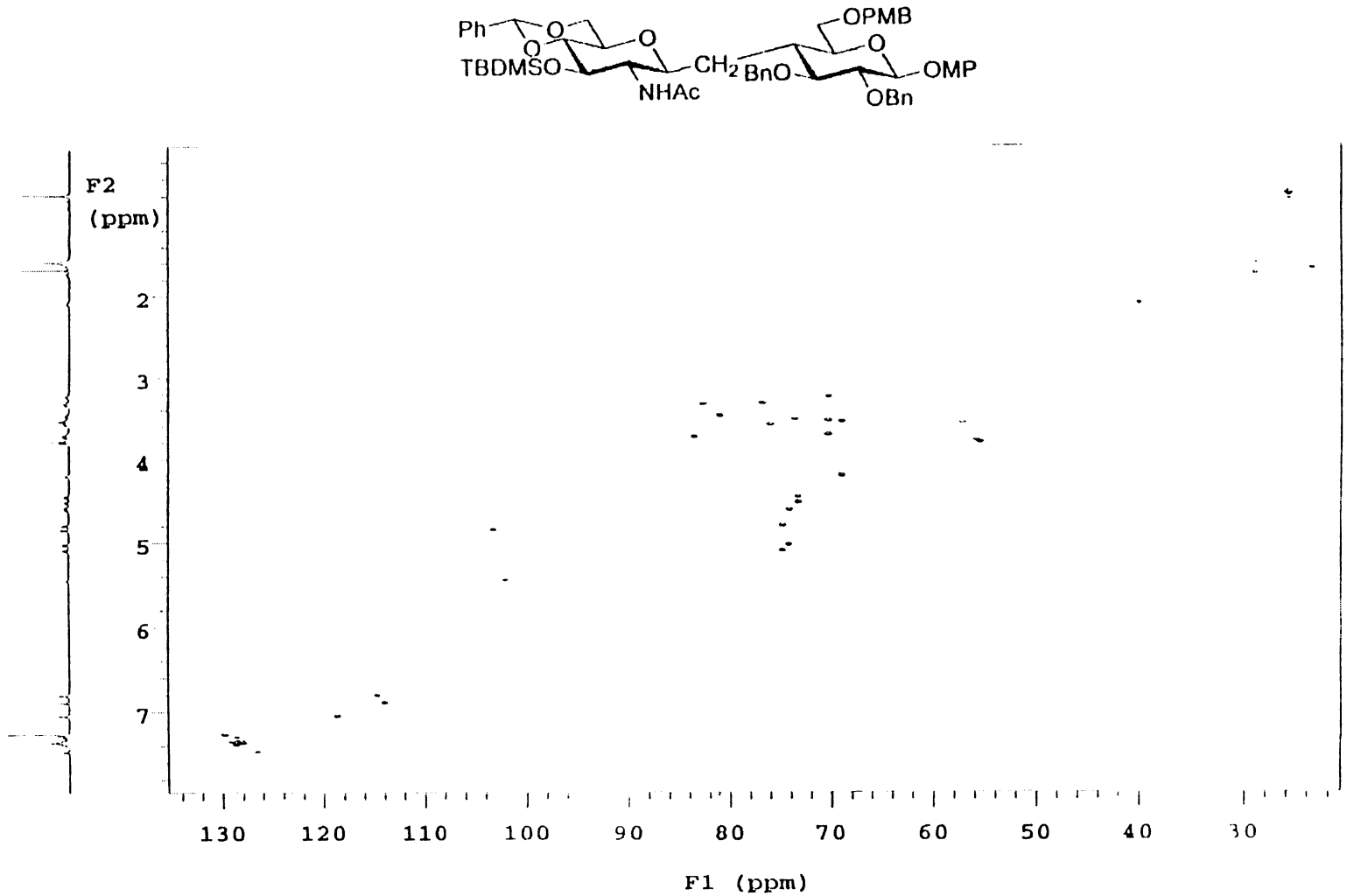
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**19**).



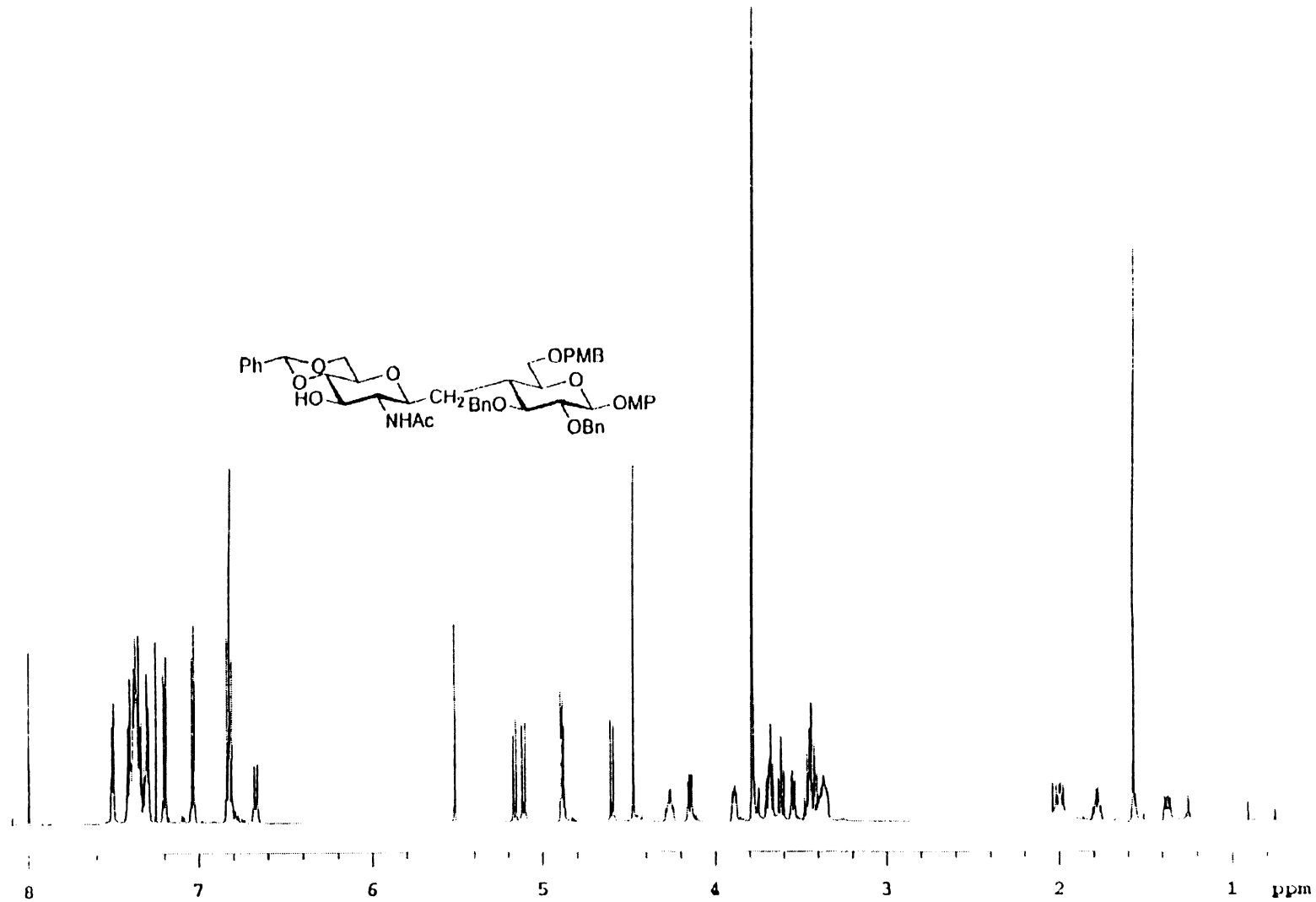
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (**19**).



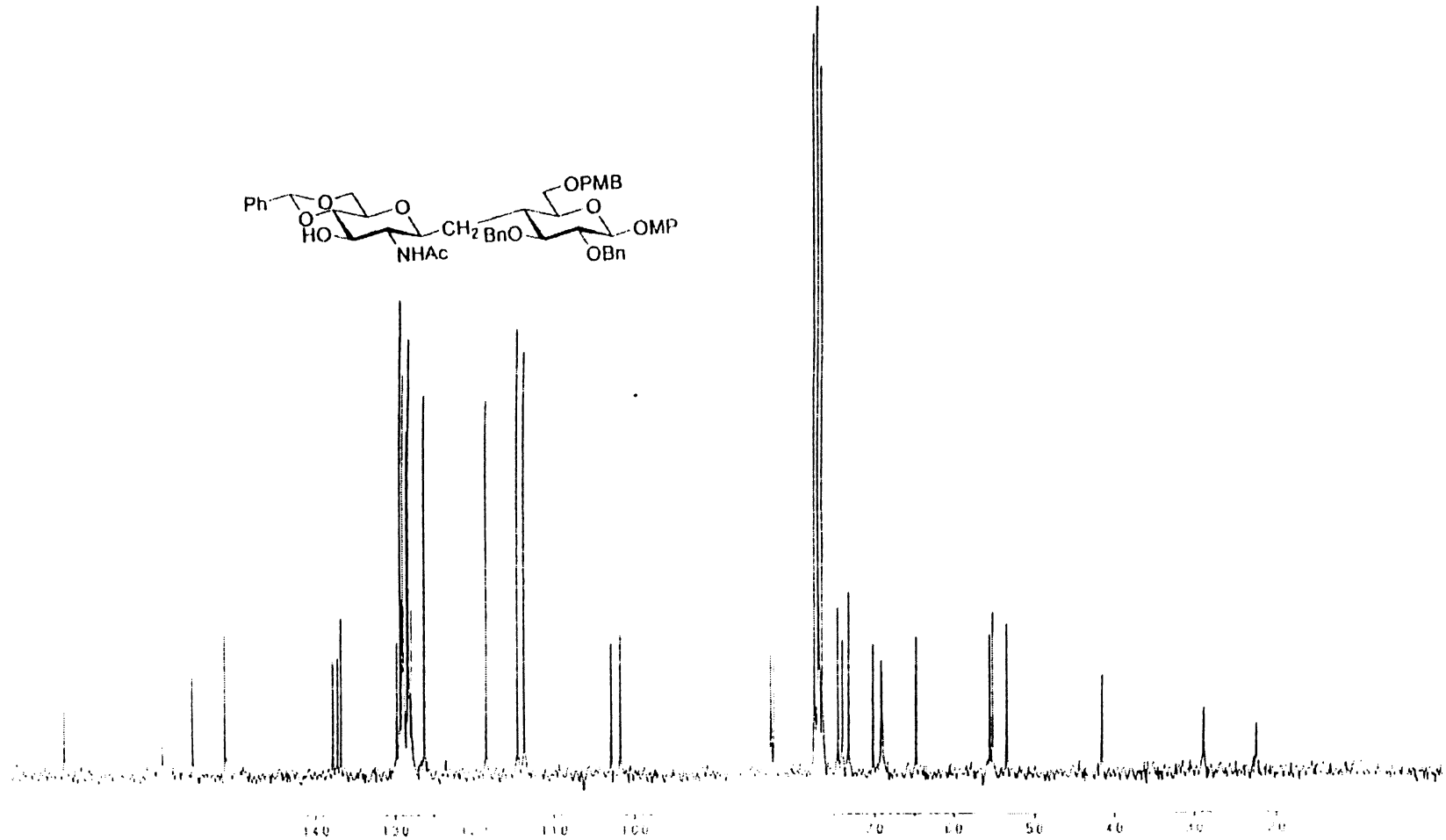
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**19**).



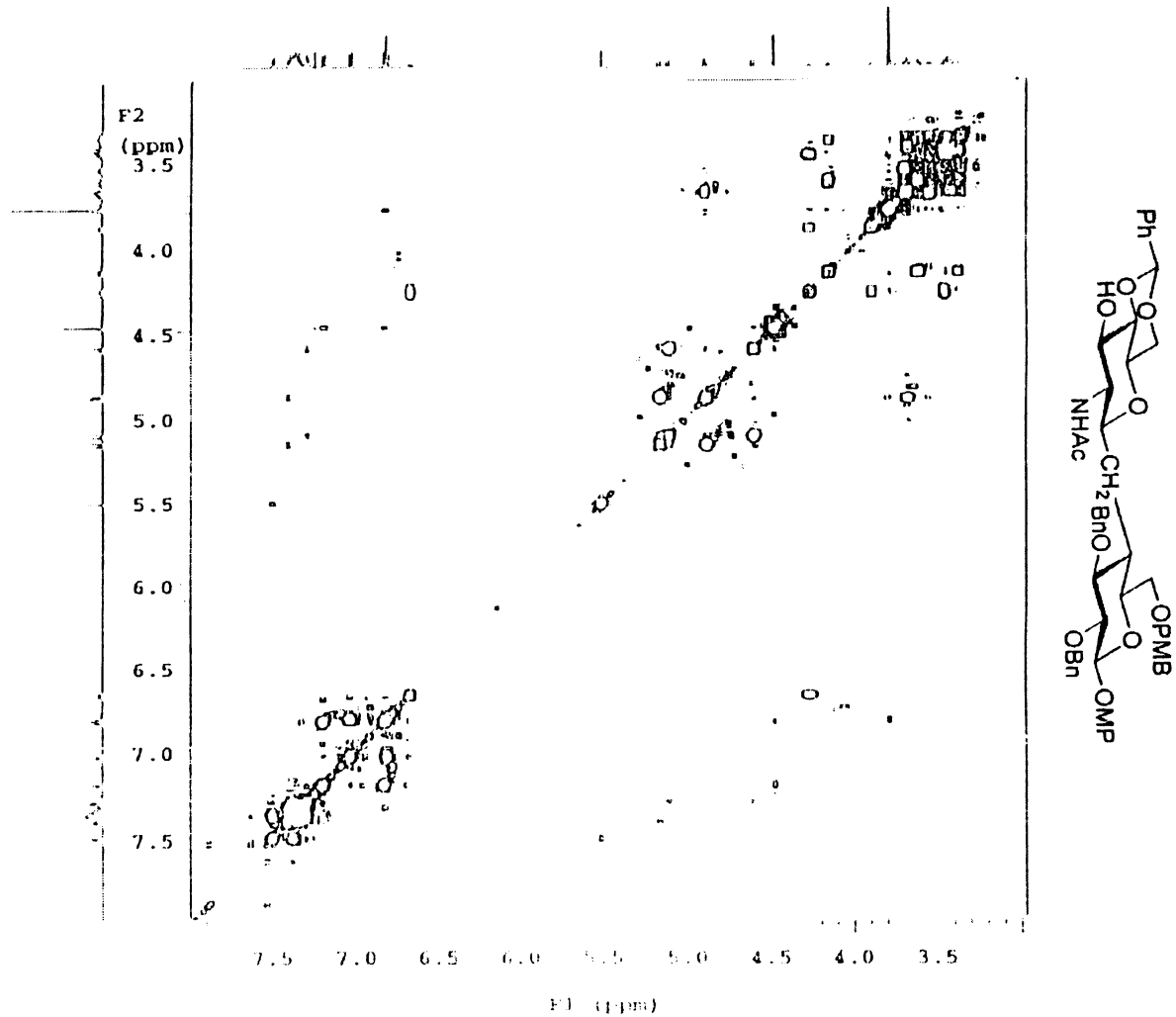
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**19**).



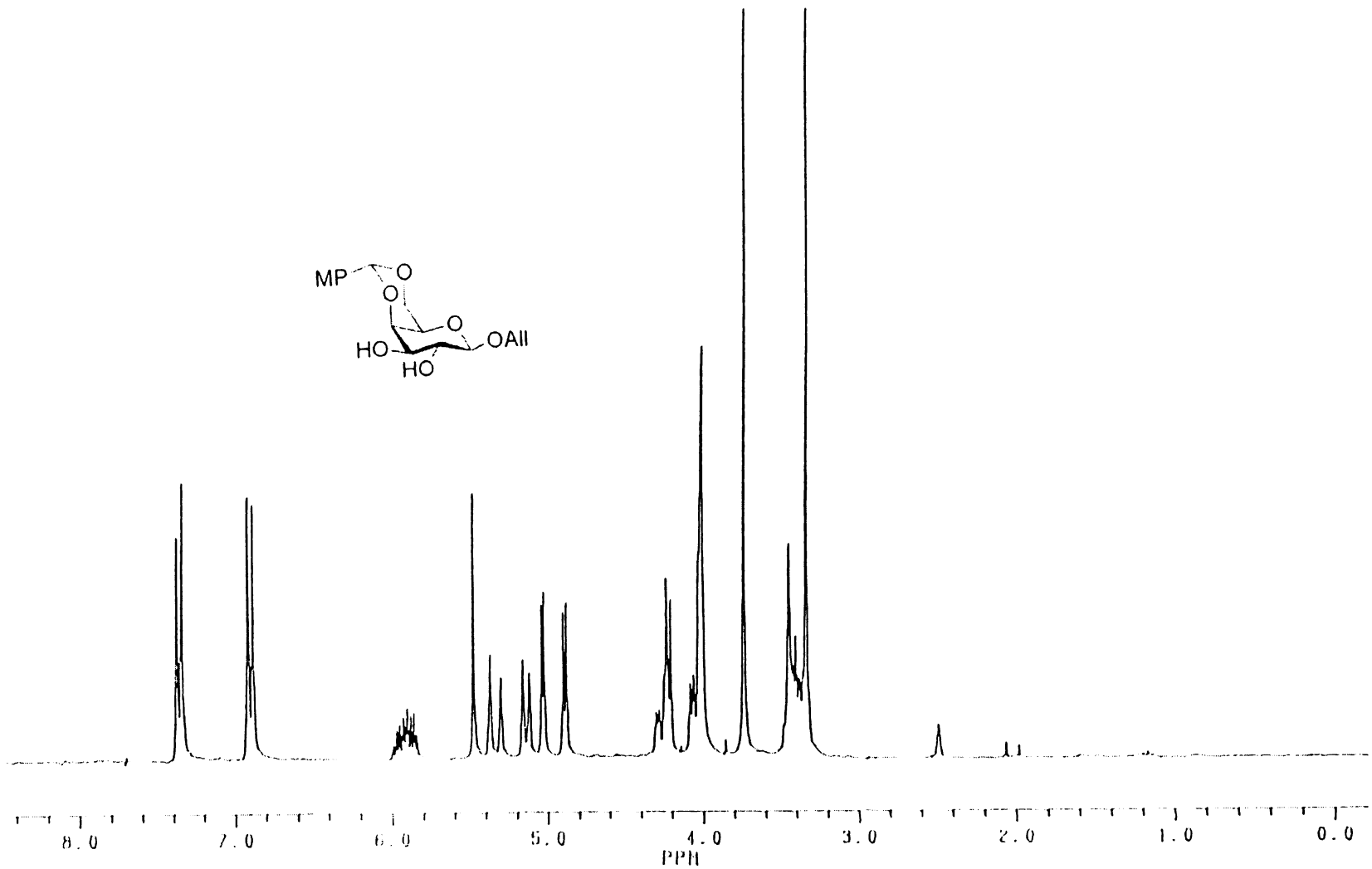
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-β-D-glucopyranoside (**84**).



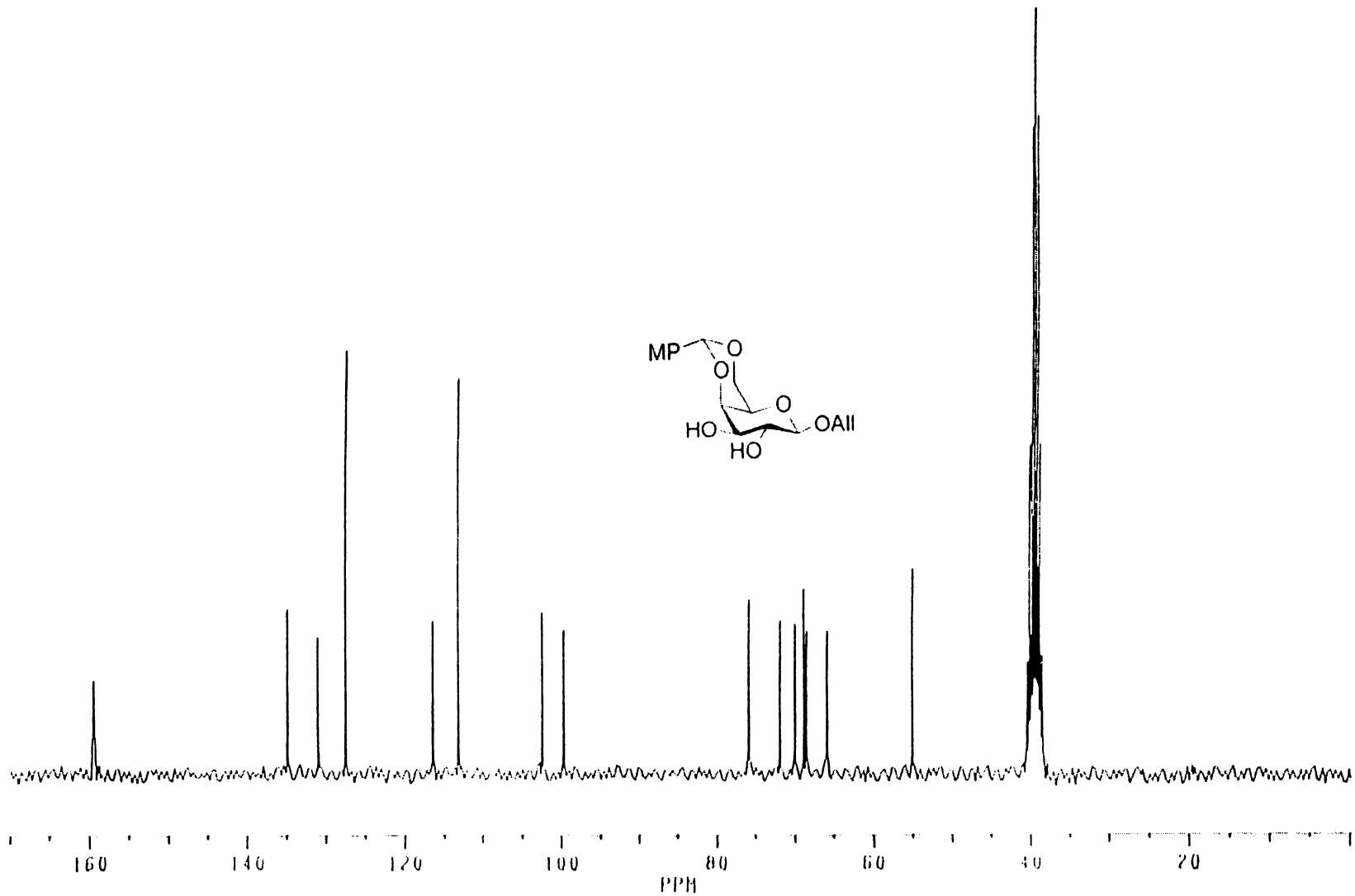
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**84**).



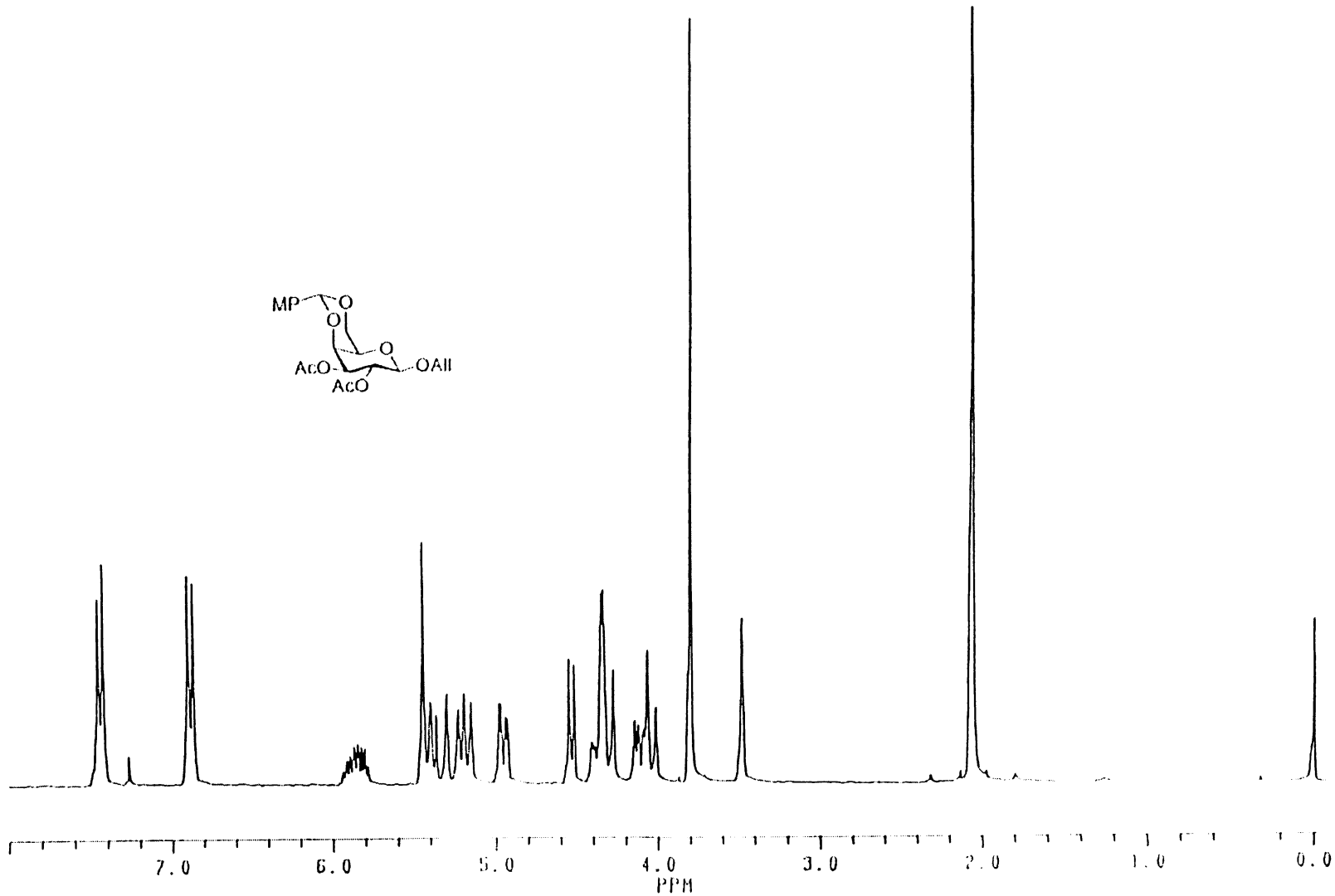
gCOSY spectrum (600 MHz, $CDCl_3$) of *p*-methoxyphenyl *C*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4a)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4a-carba-*β*-D-glucopyranoside (**84**).



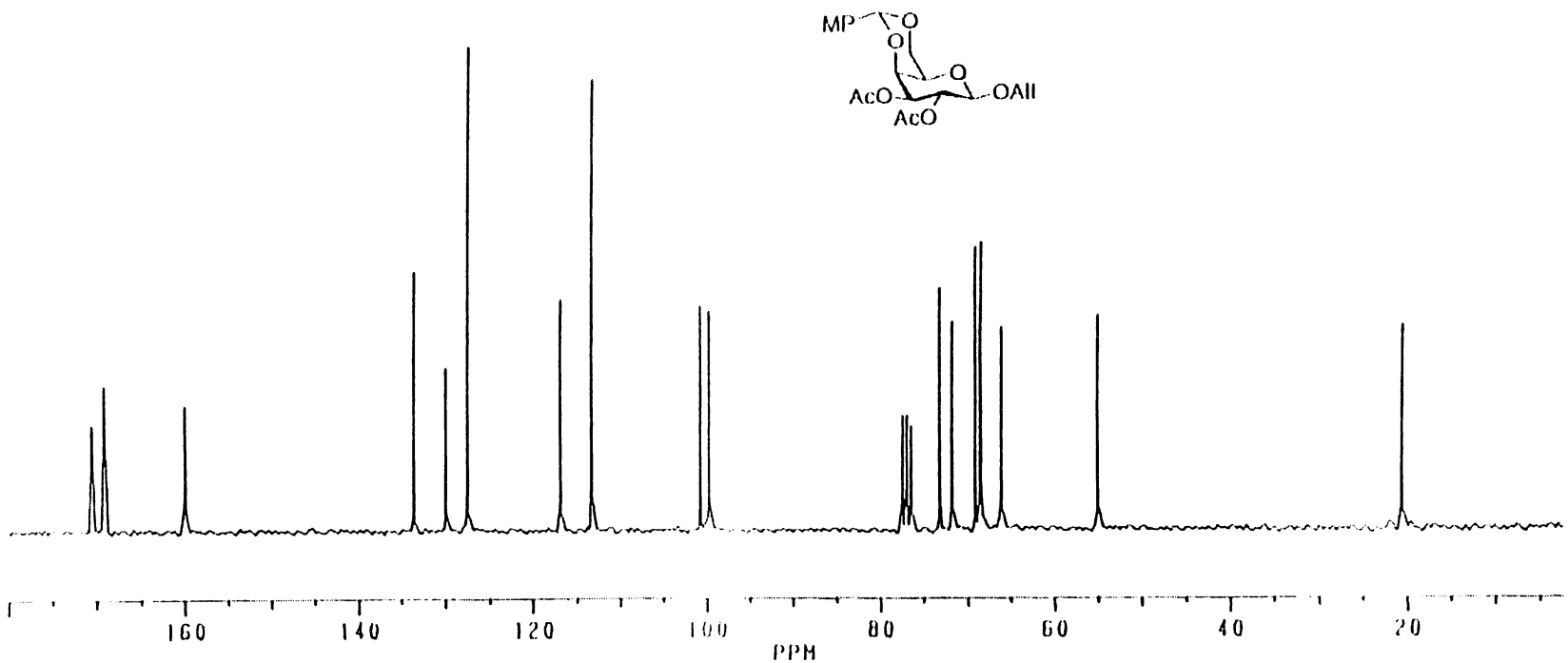
^{1}H NMR spectrum (250 MHz, DMSO-d_6) of allyl 4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**100**).



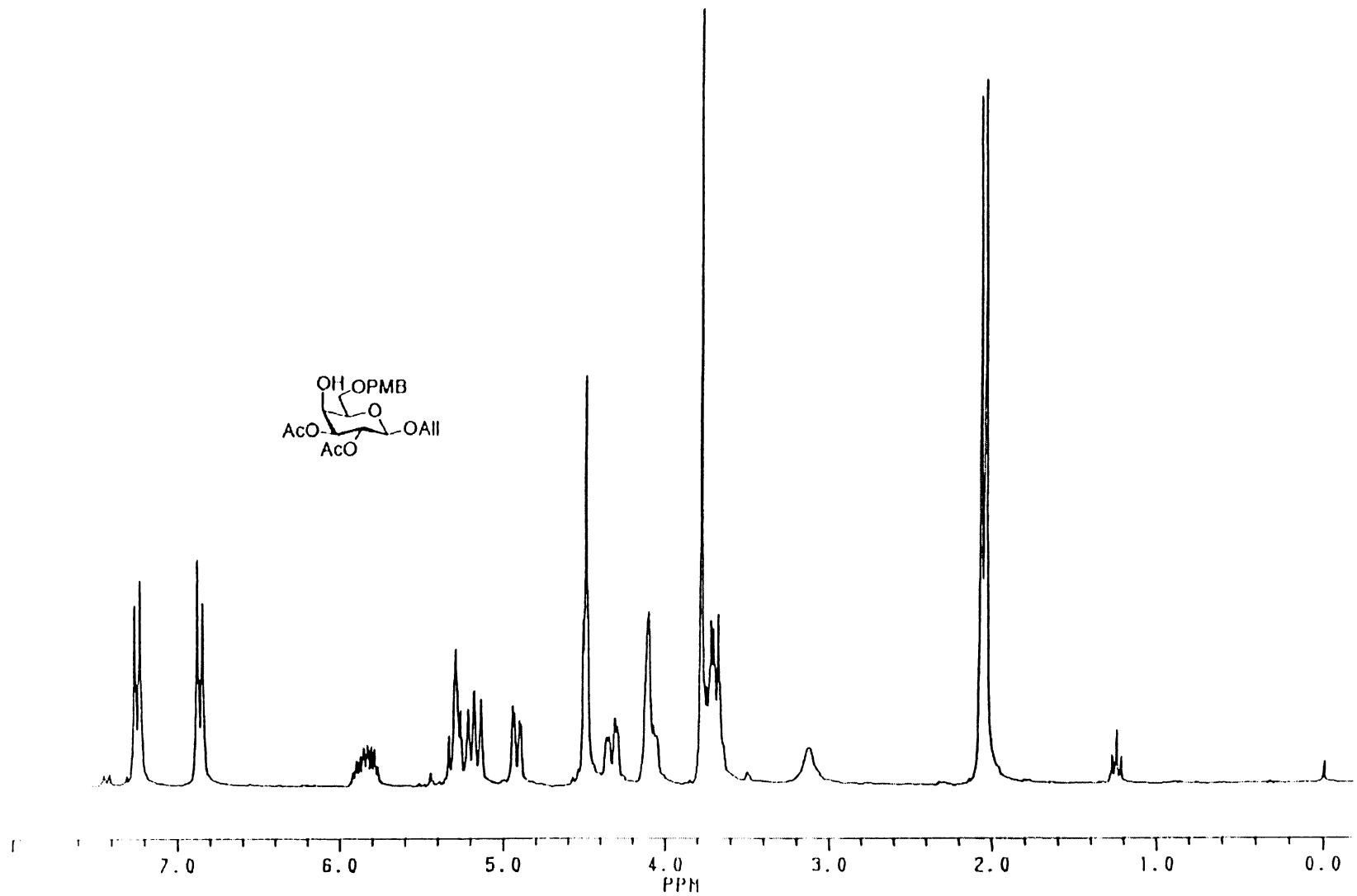
^{13}C NMR spectrum (62.5 MHz, DMSO-d_6) of allyl 4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (100).



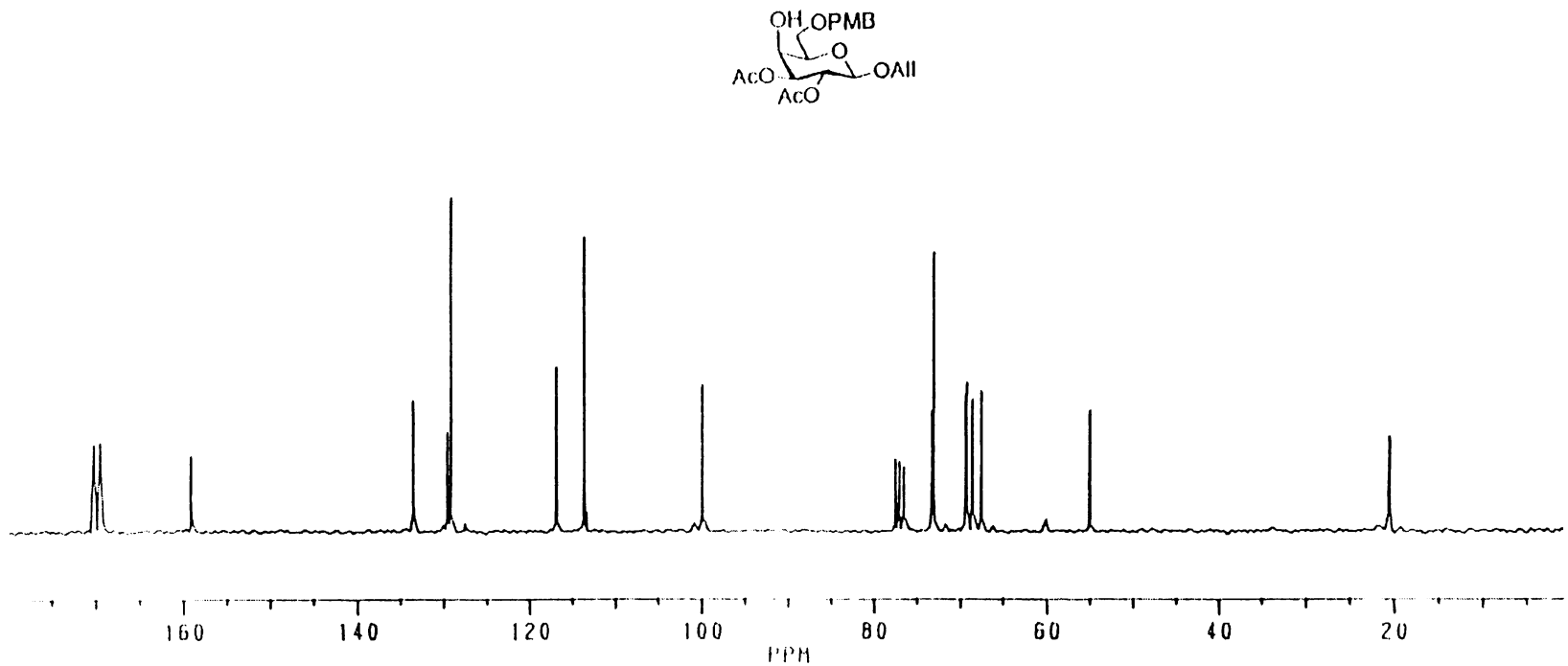
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**101**).



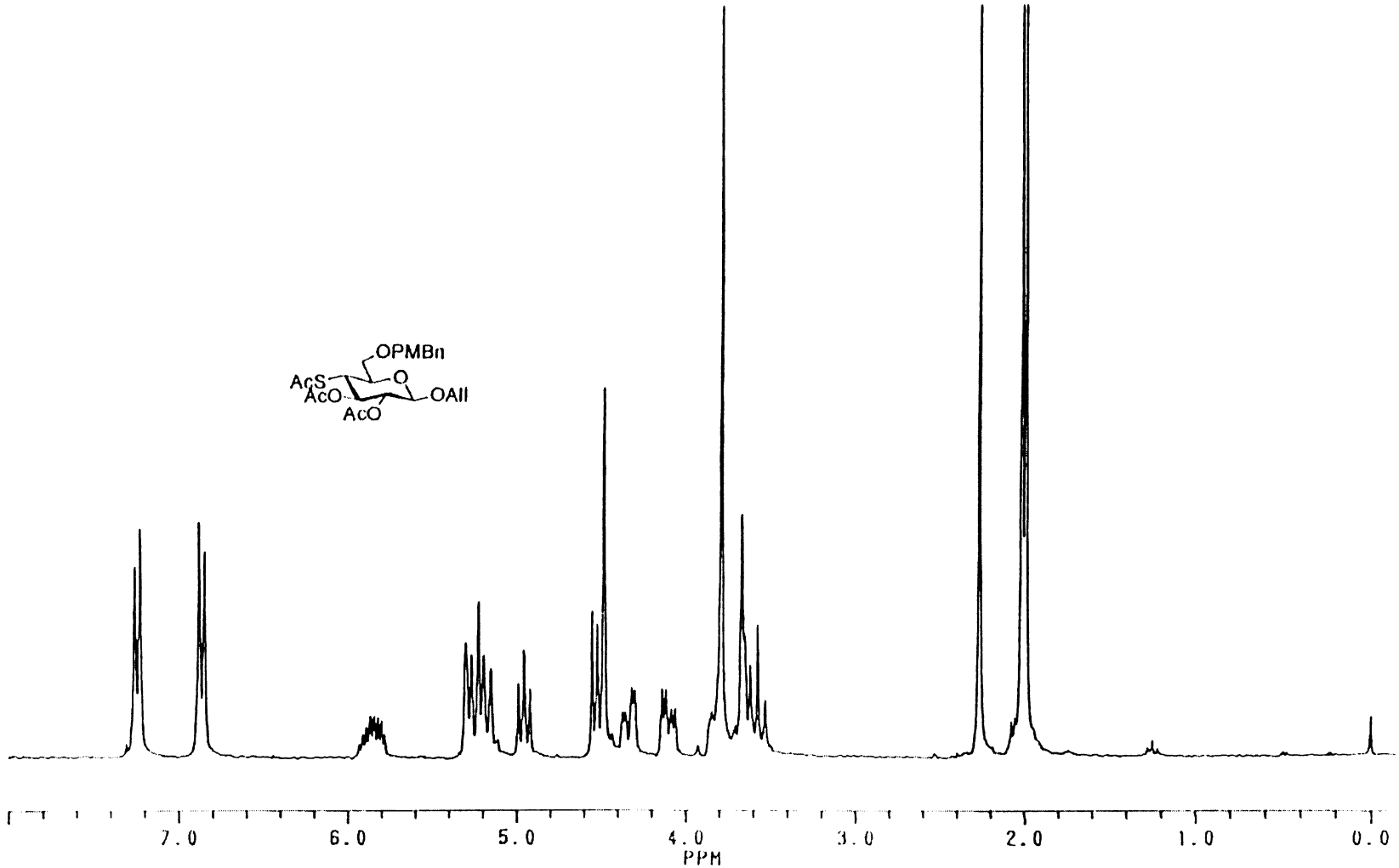
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-4,6-*O*-*p*-methoxybenzylidene-*β*-D-galactopyranoside (**101**).



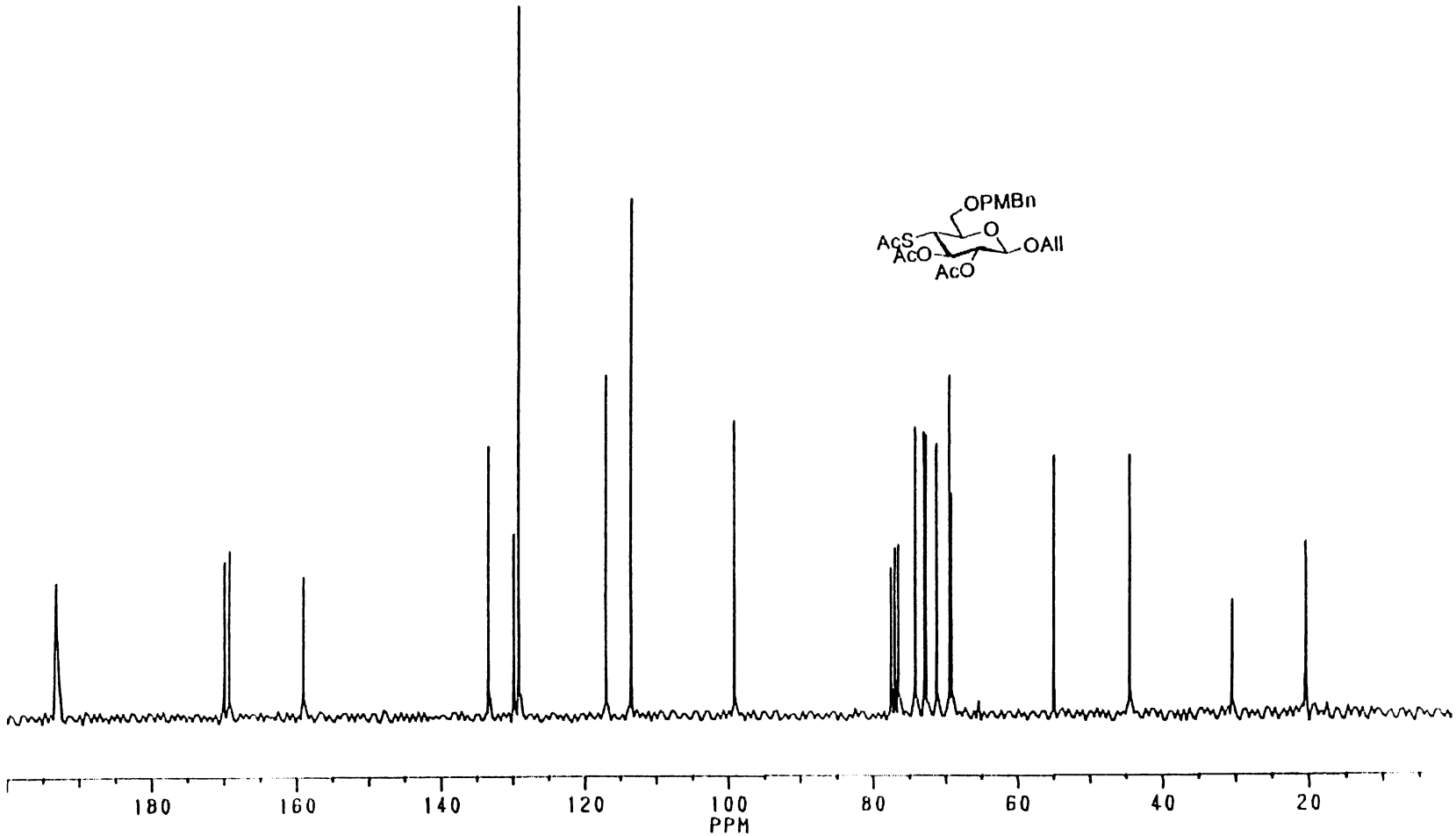
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (**102**).



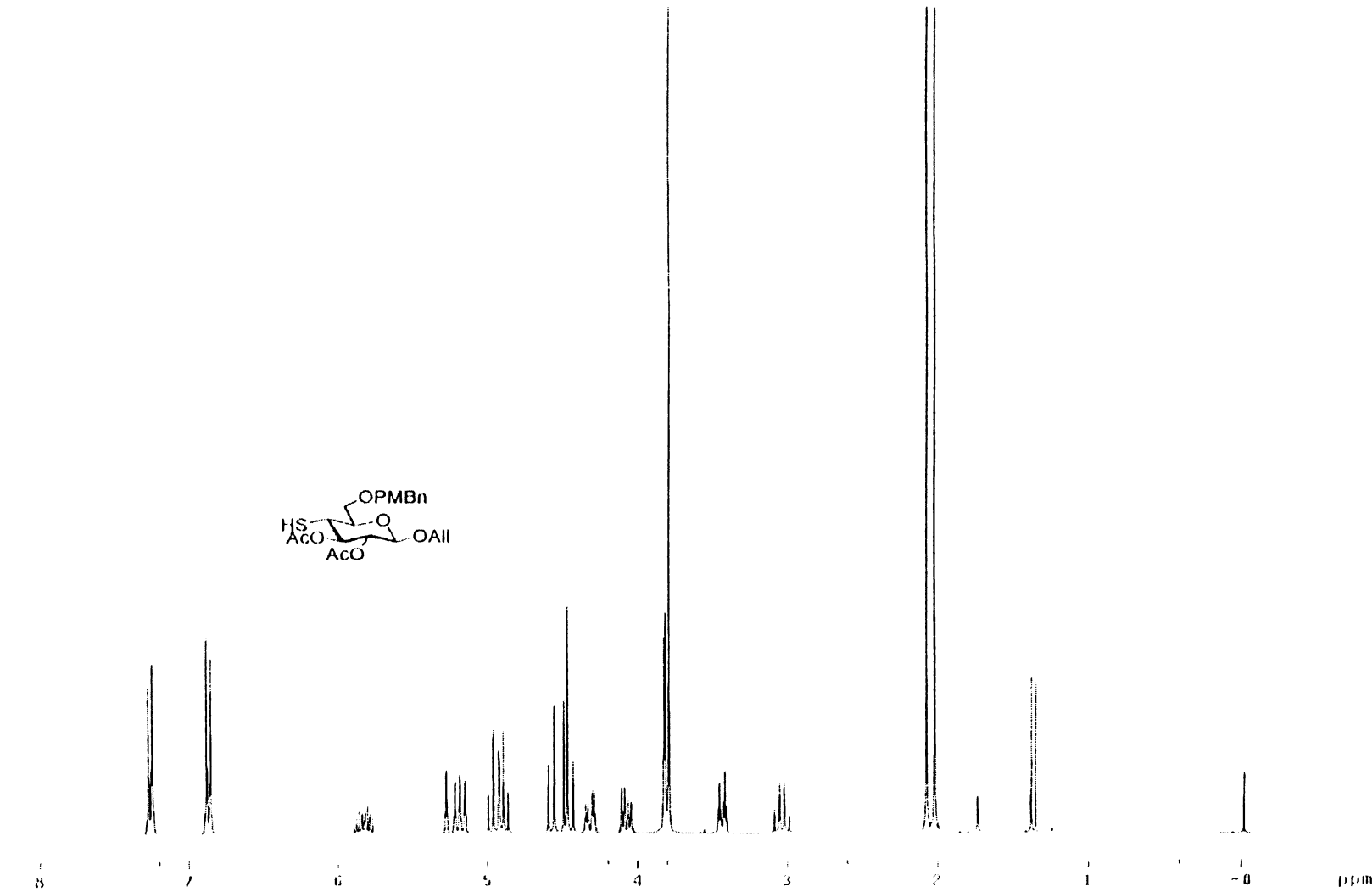
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-*β*-D-galactopyranoside (**102**).



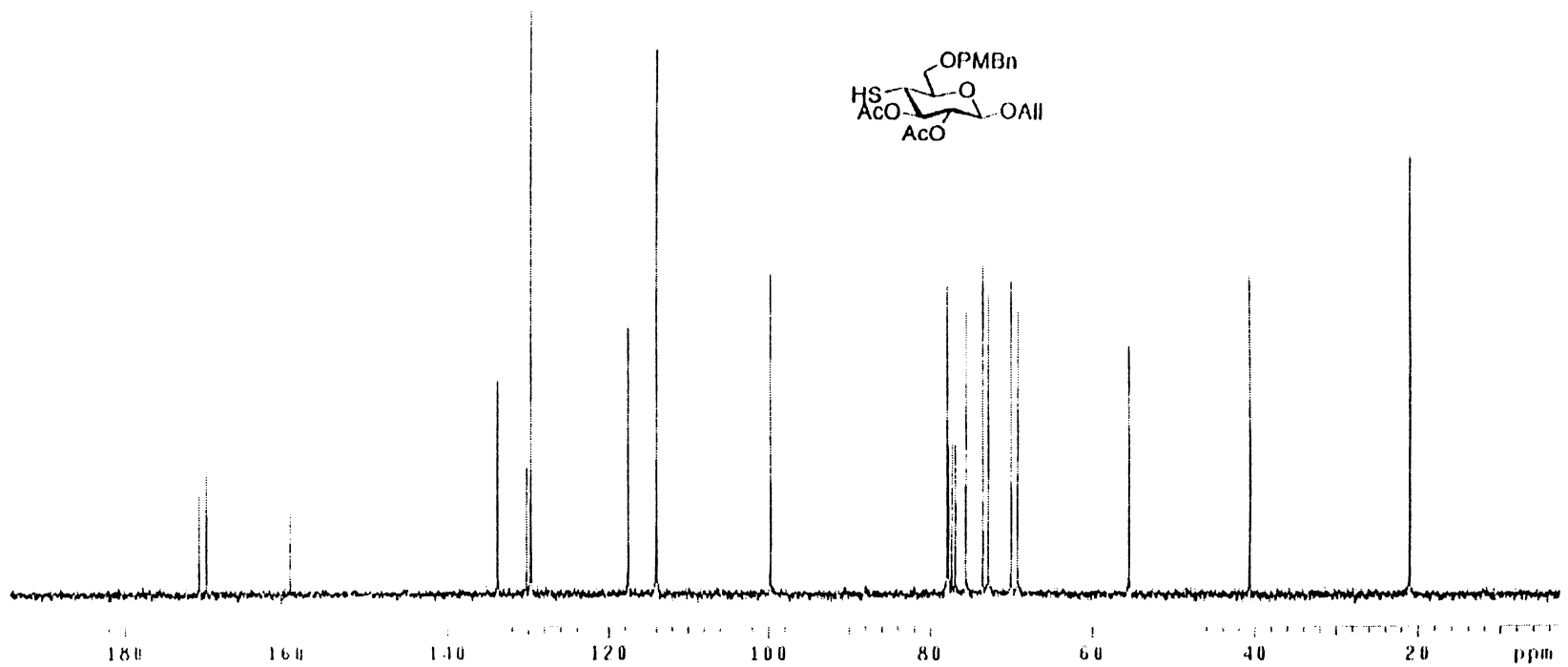
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (**104**).



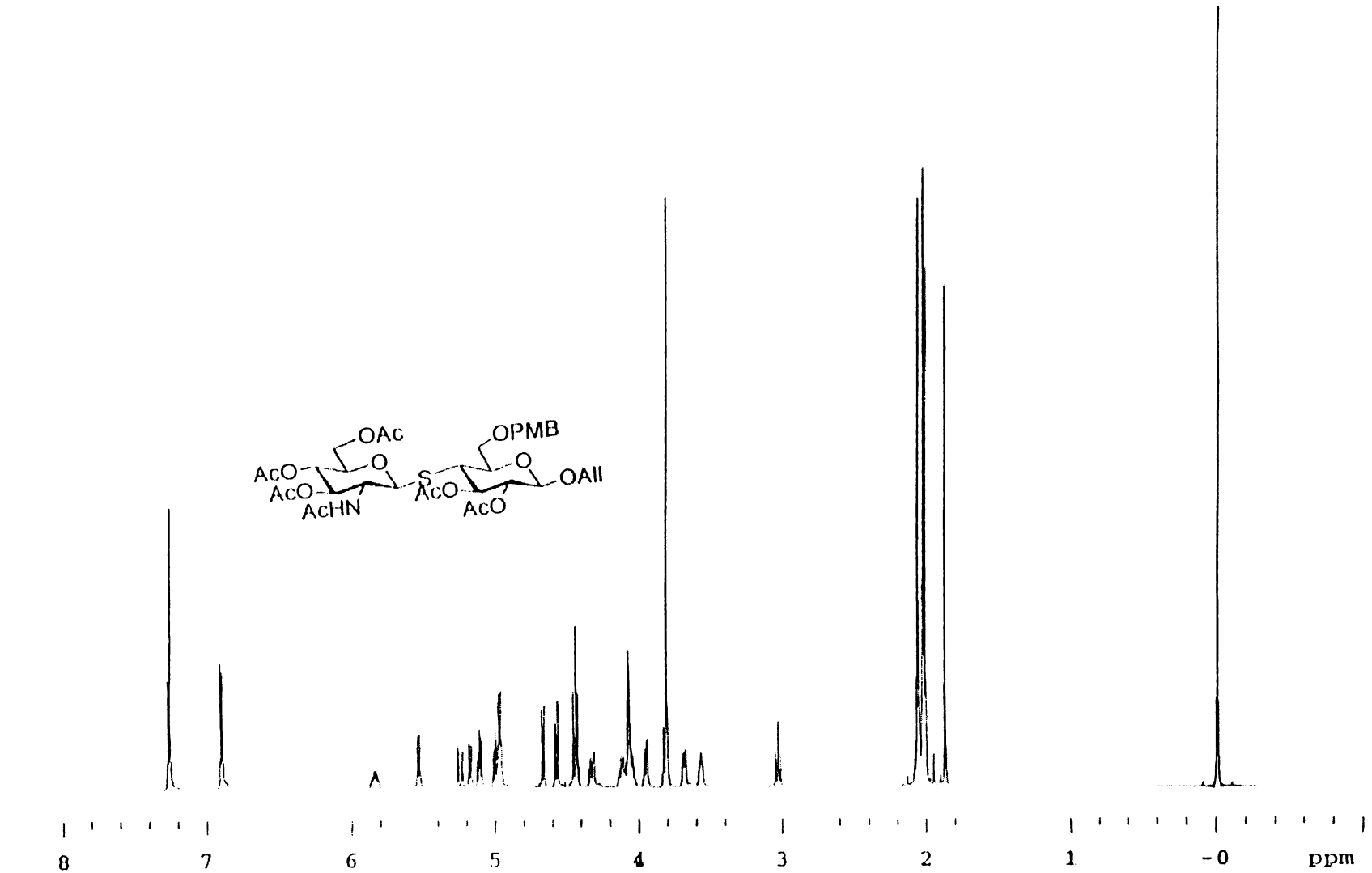
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (**104**).



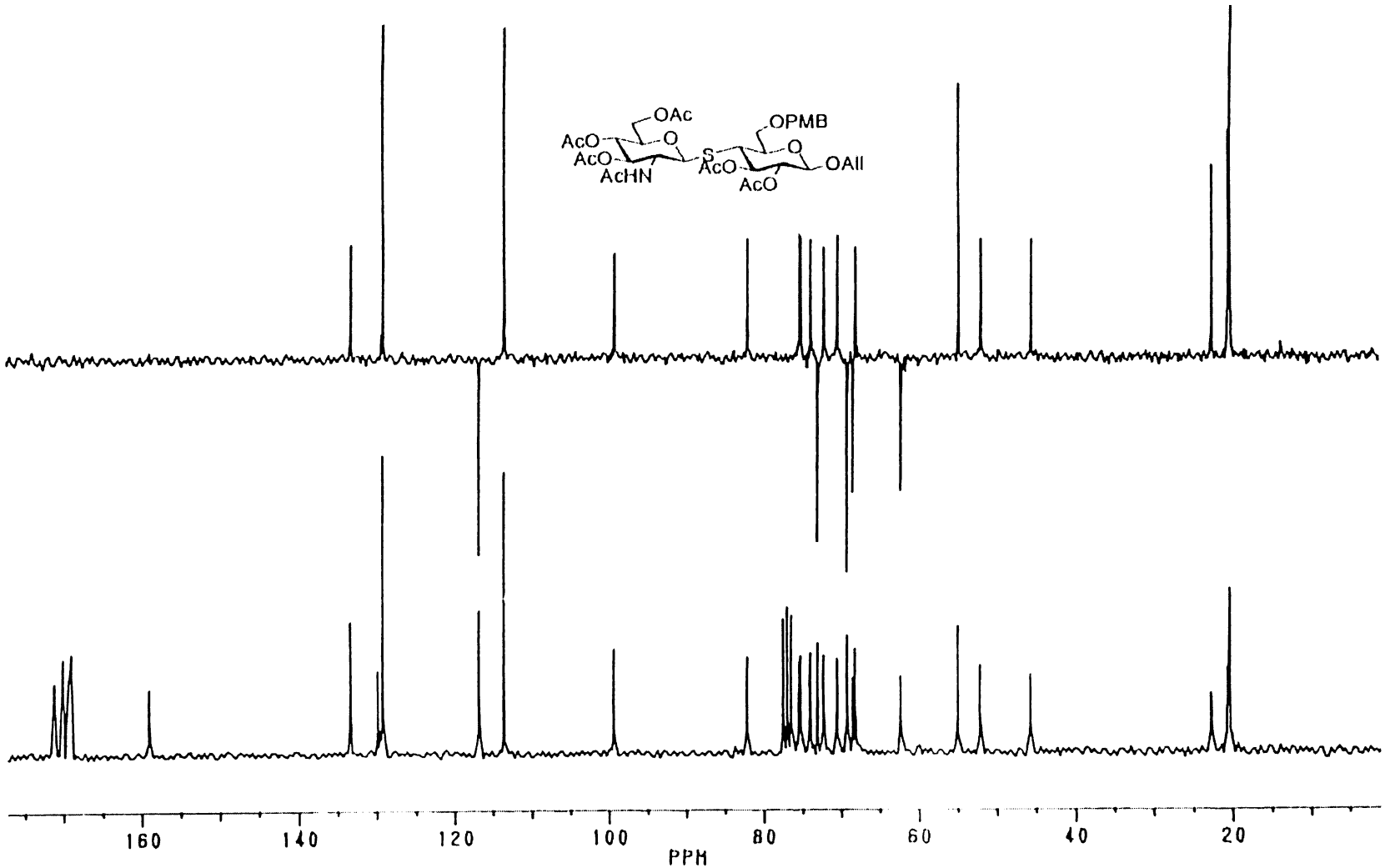
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (**105**).



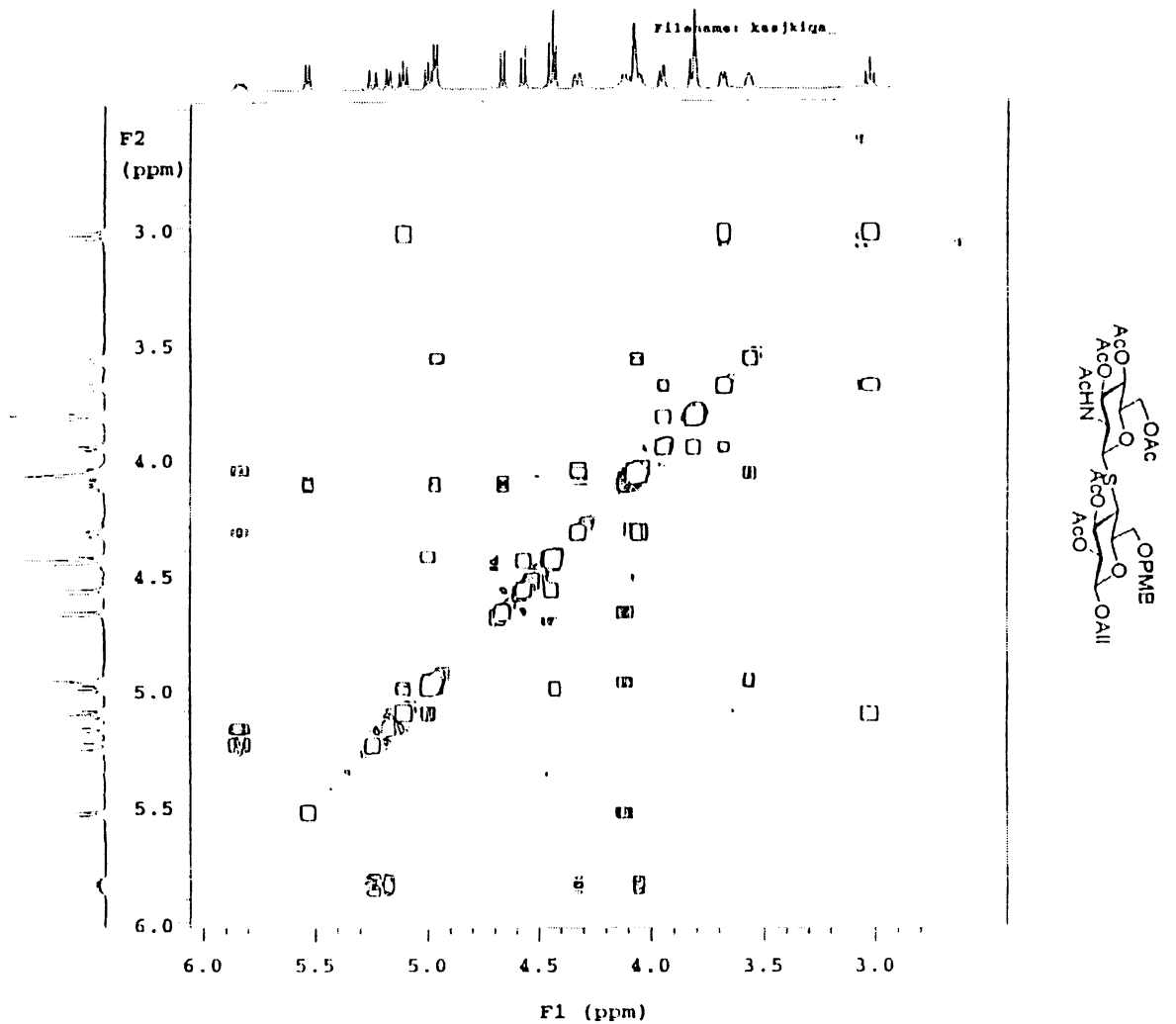
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of allyl 2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-galactopyranoside (**105**).



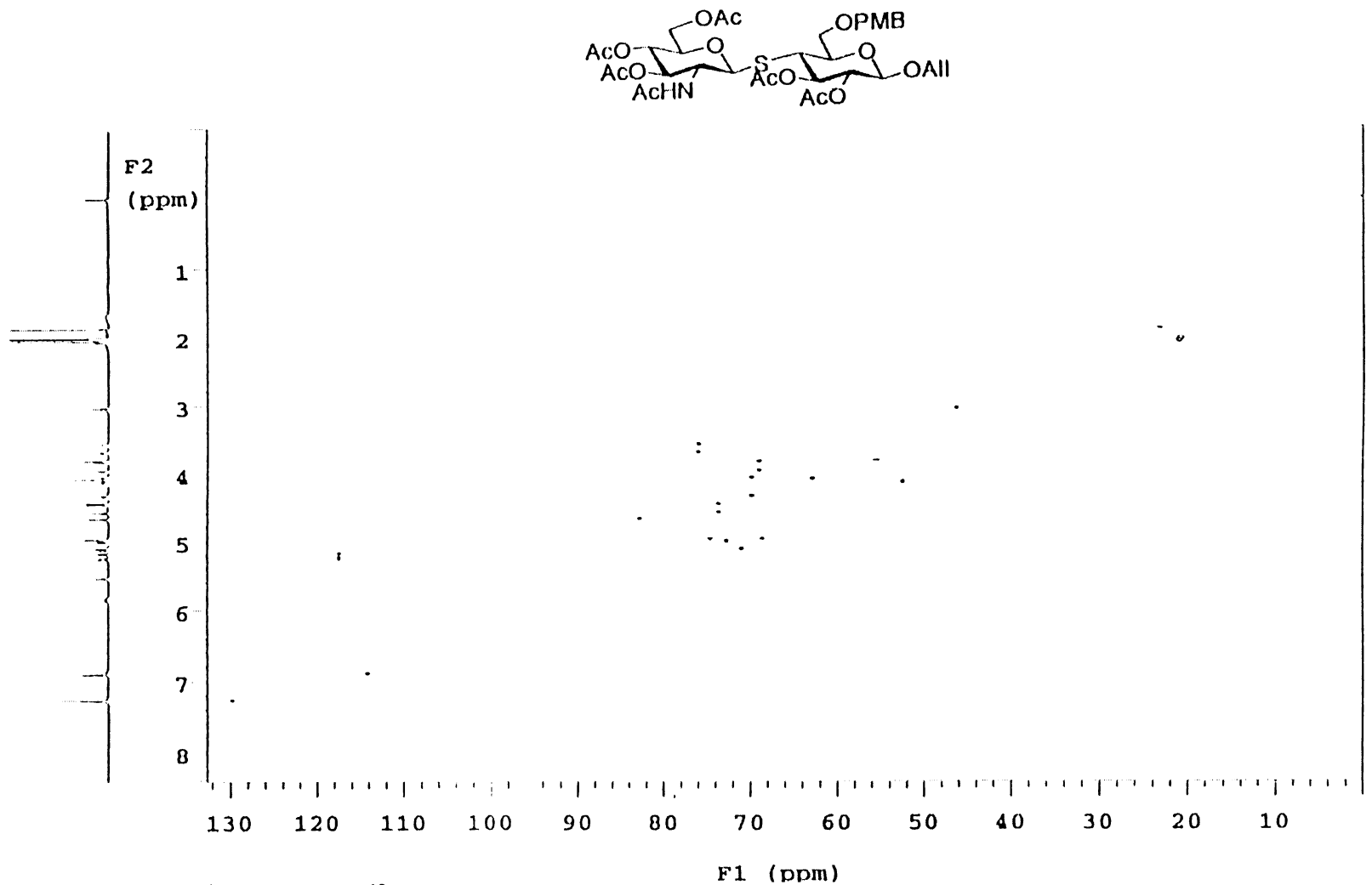
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**56**).



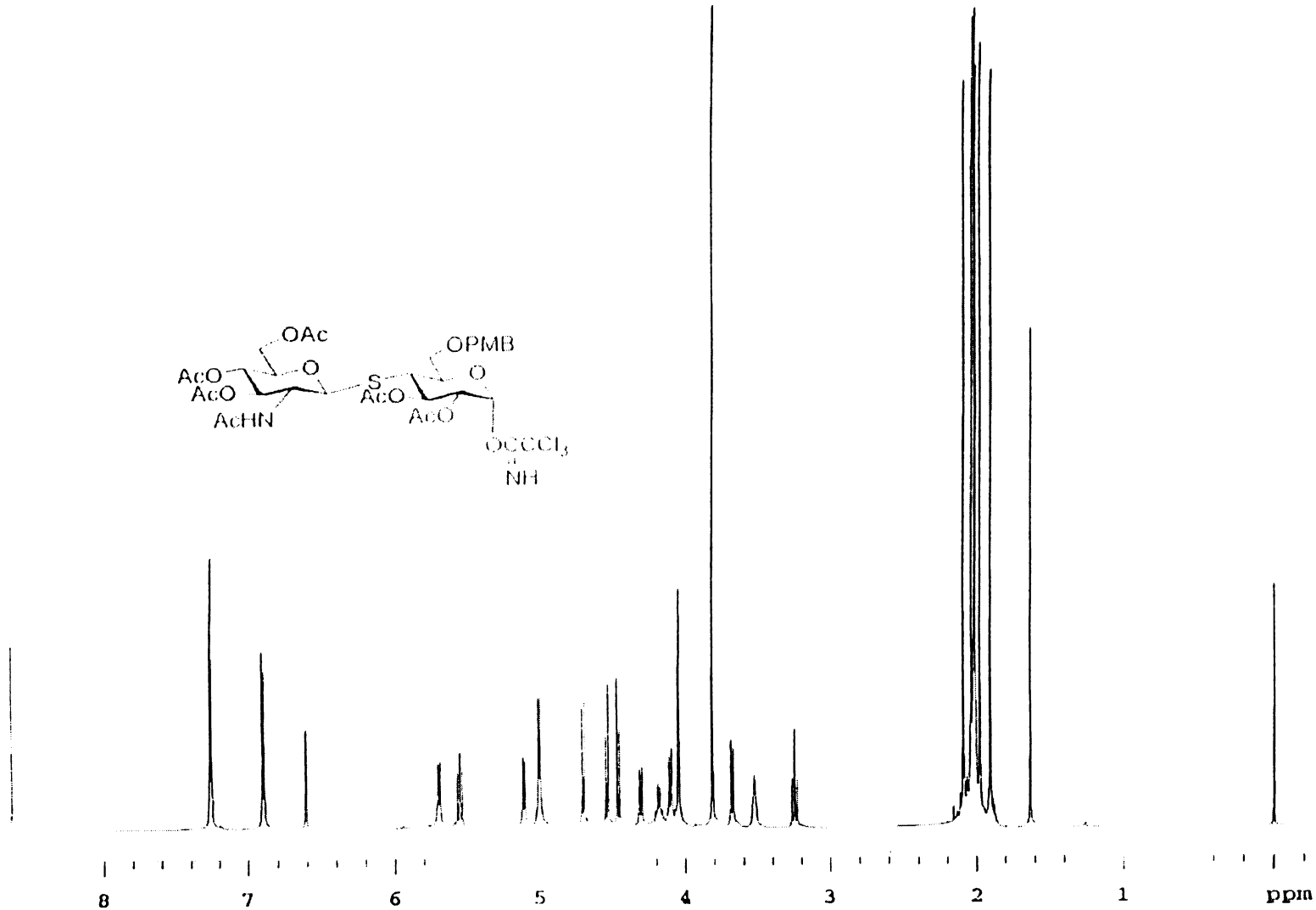
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**56**).



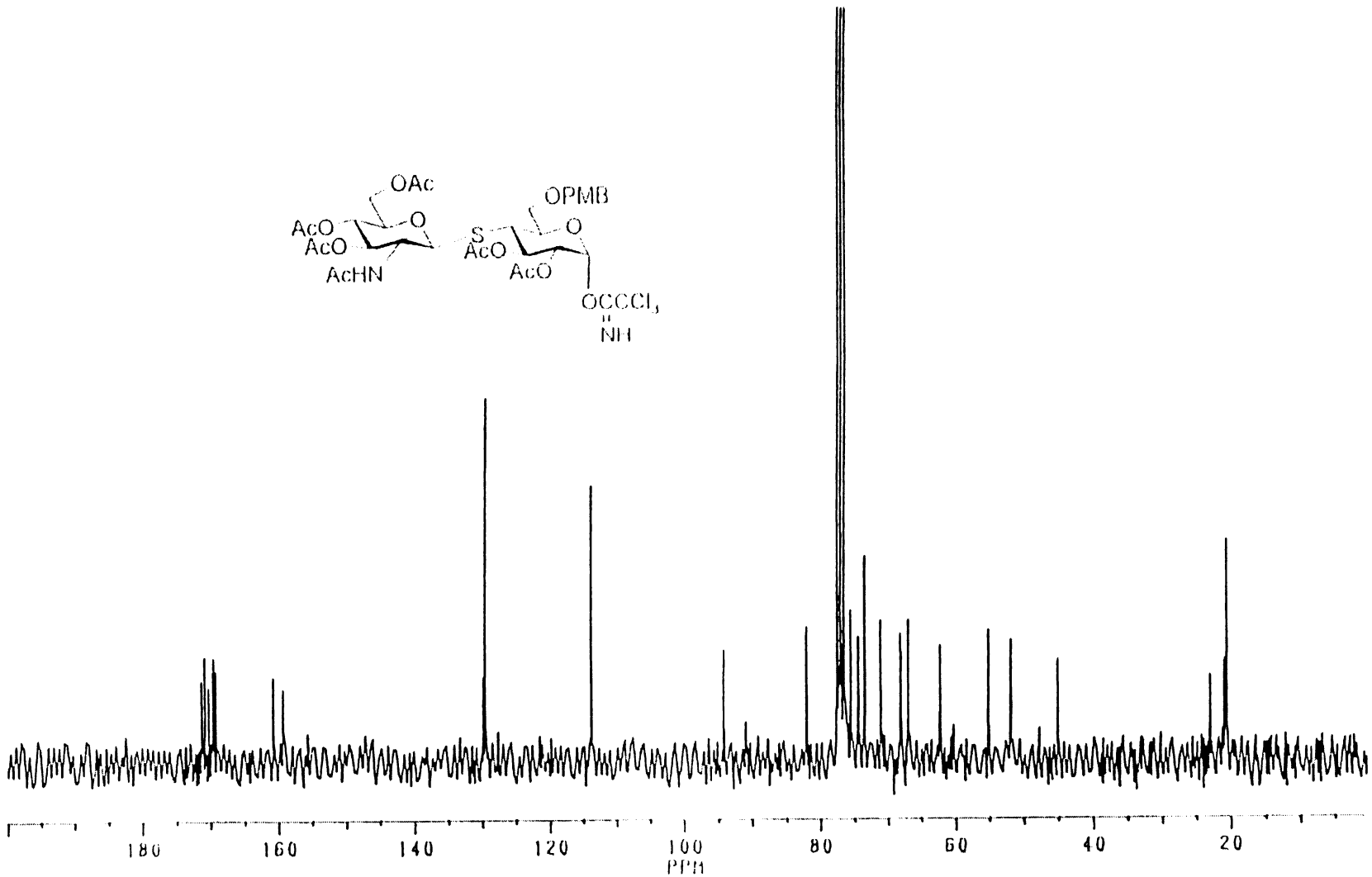
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**56**).



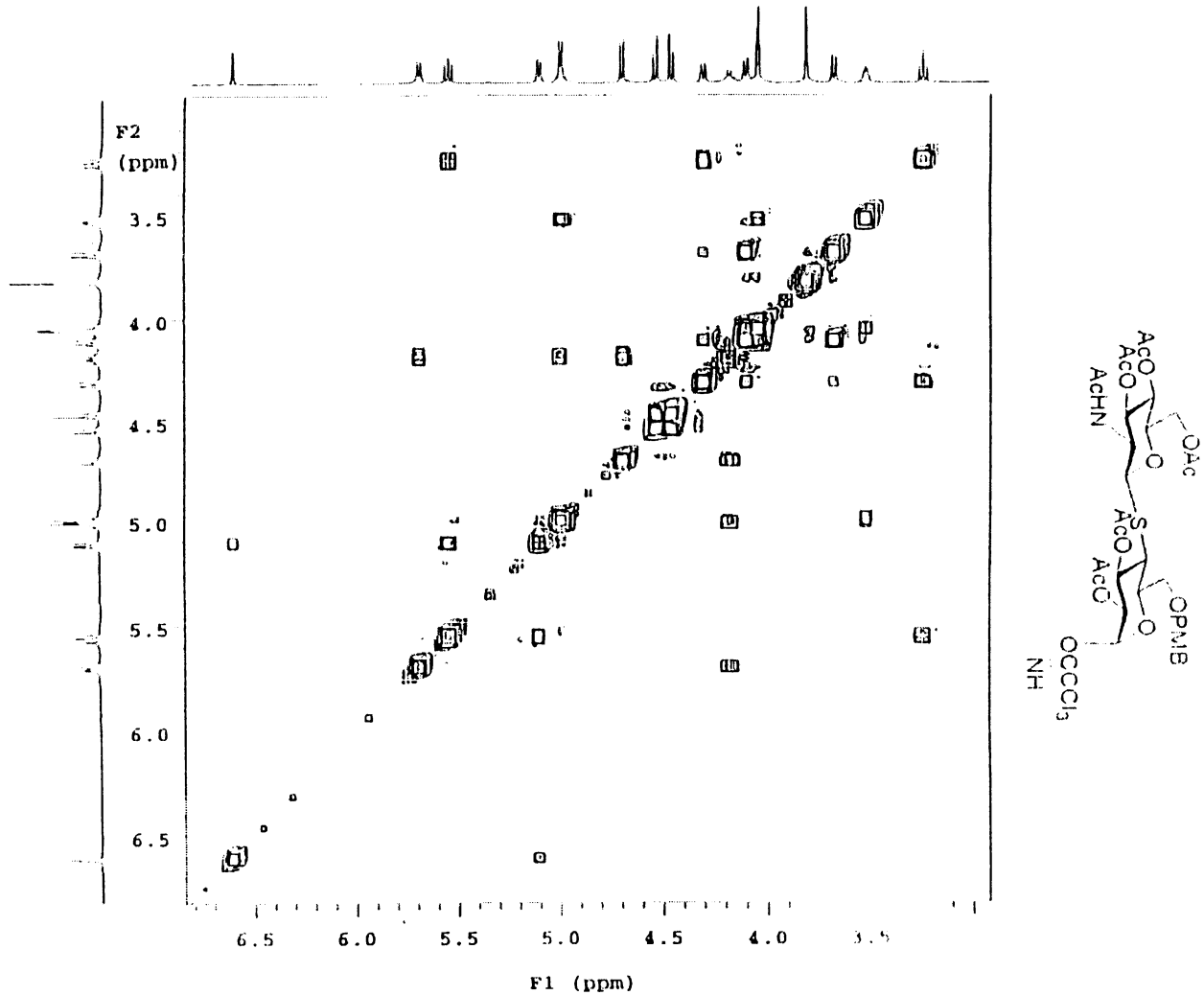
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**56**).



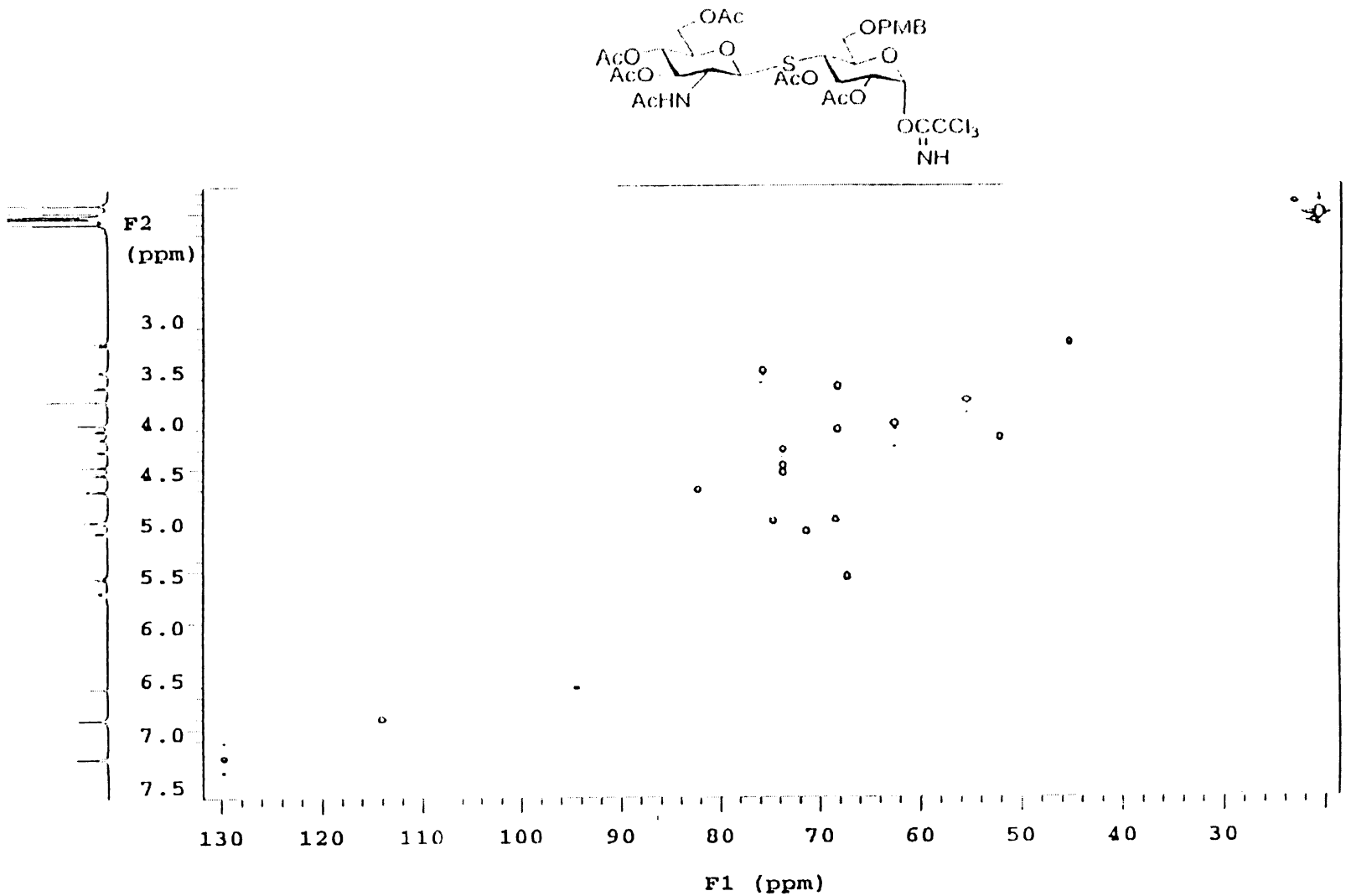
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**54**).



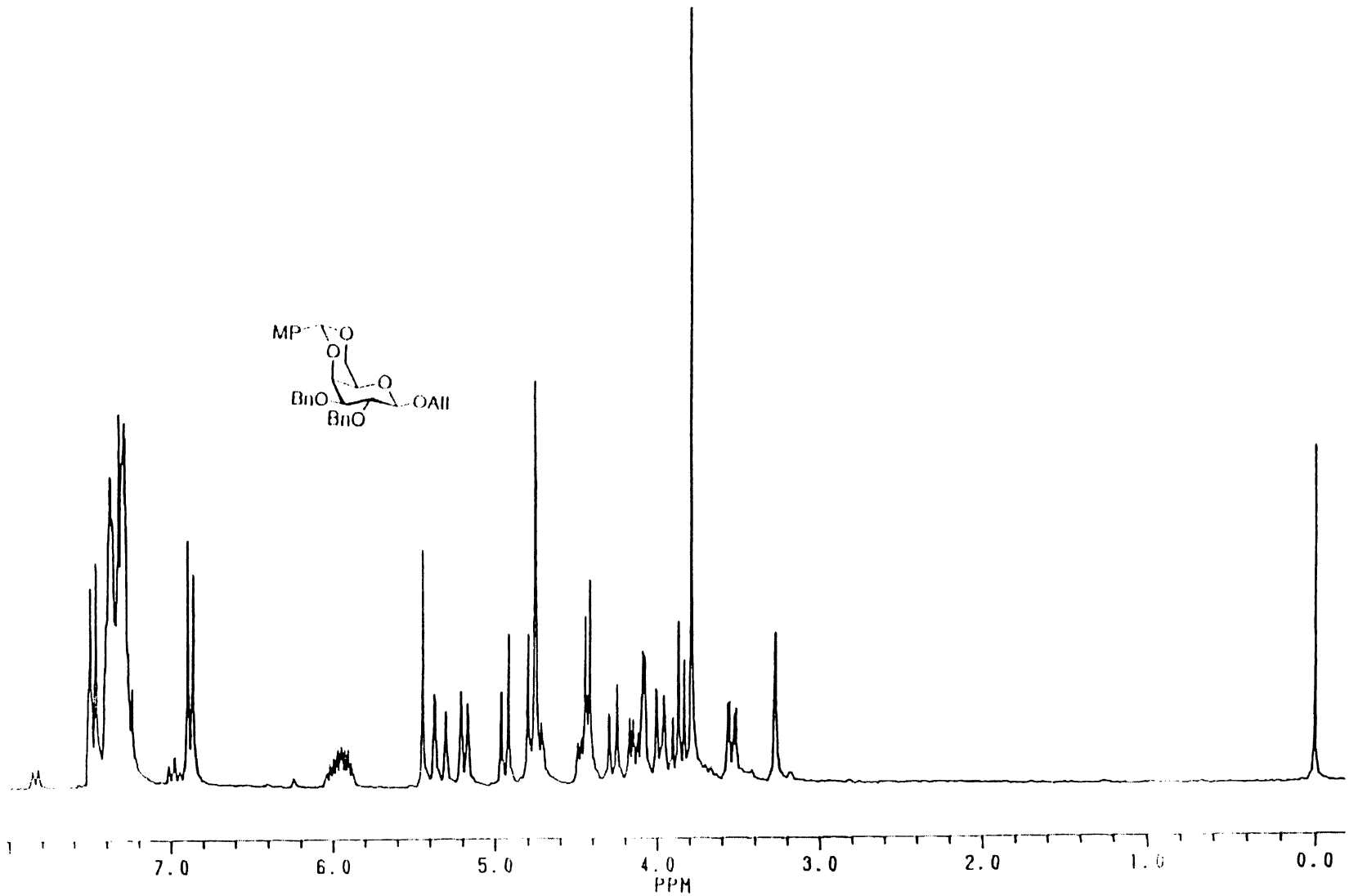
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**54**).



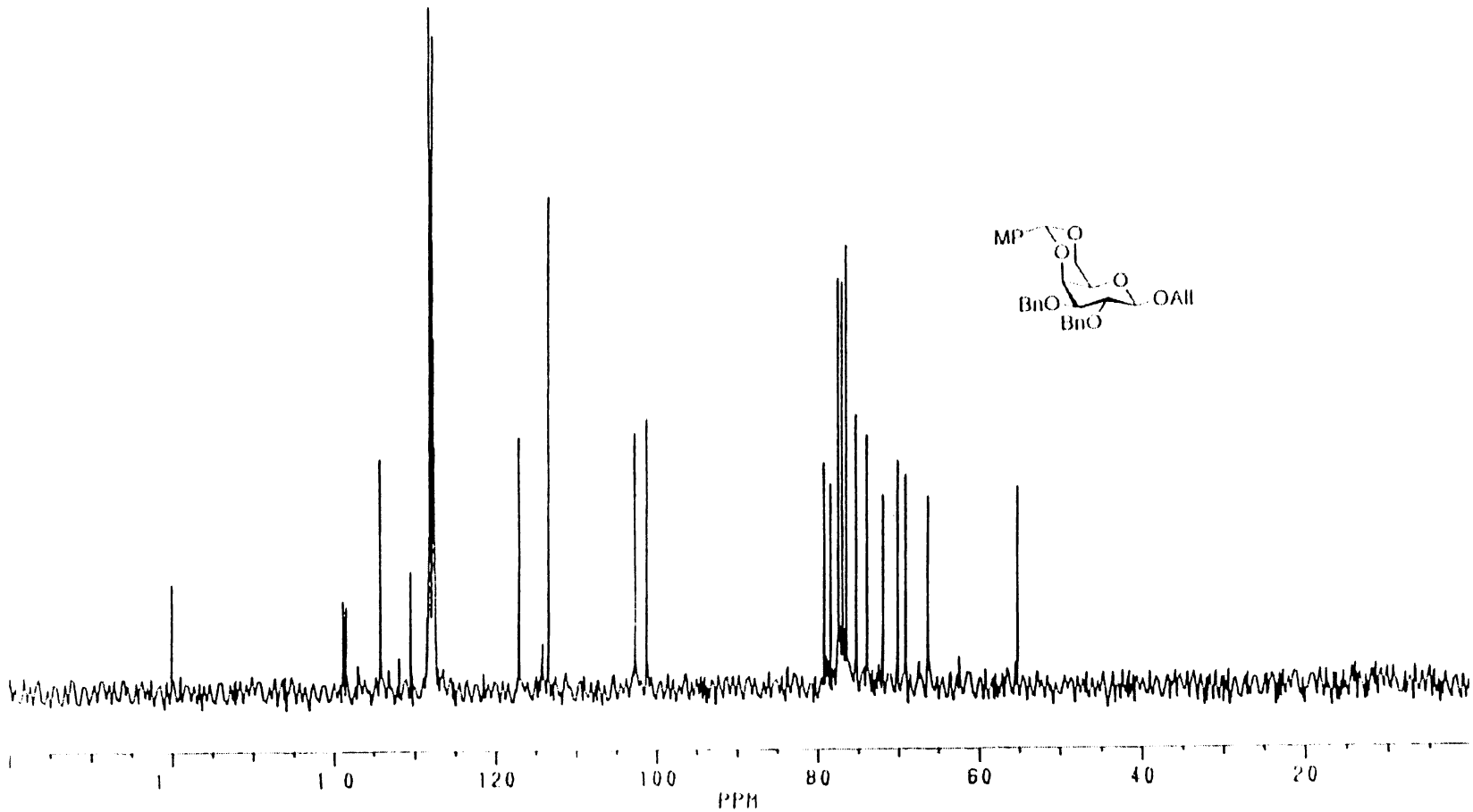
gCOSY spectrum (600 MHz, $CDCl_3$) of *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**54**).



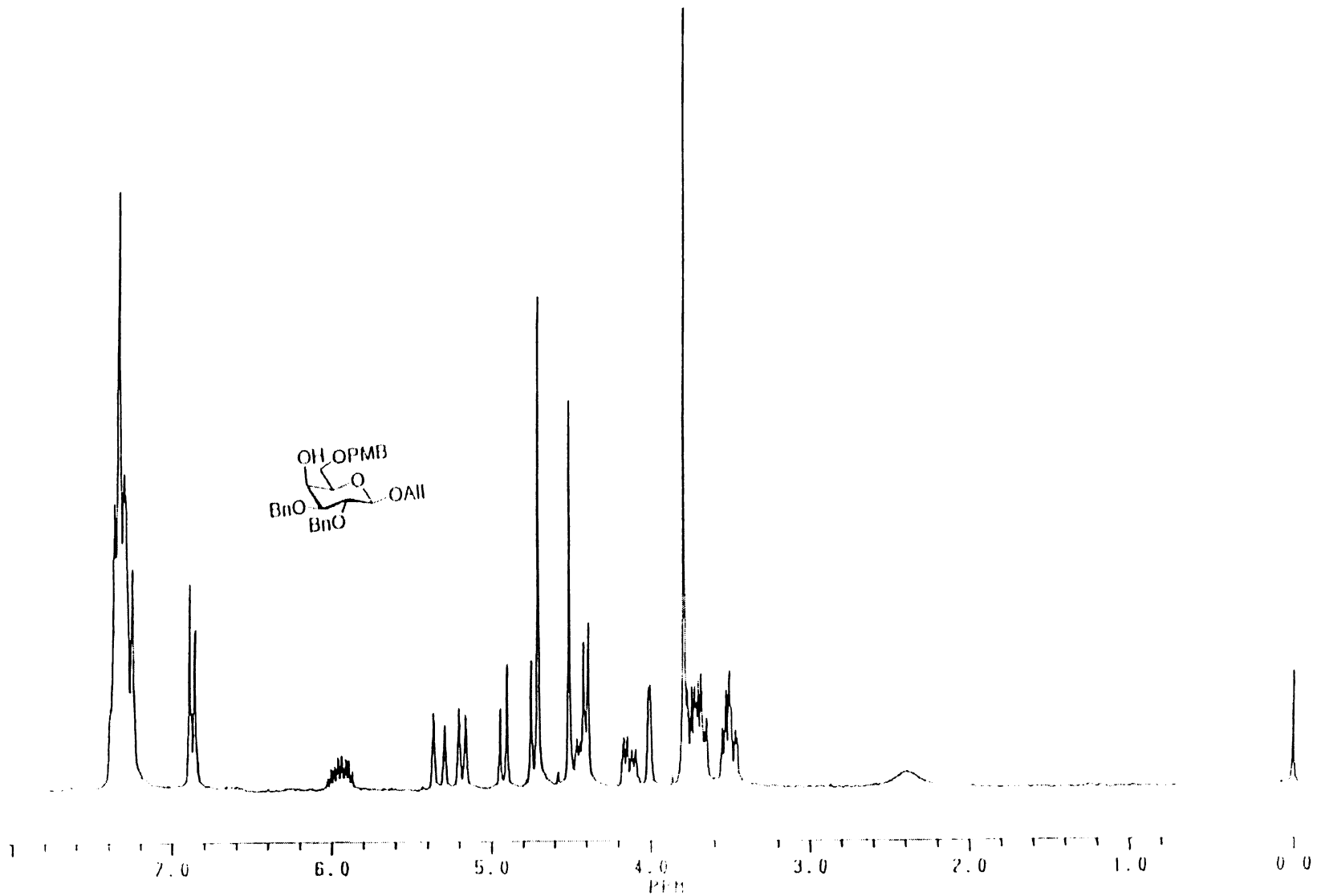
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**54**).



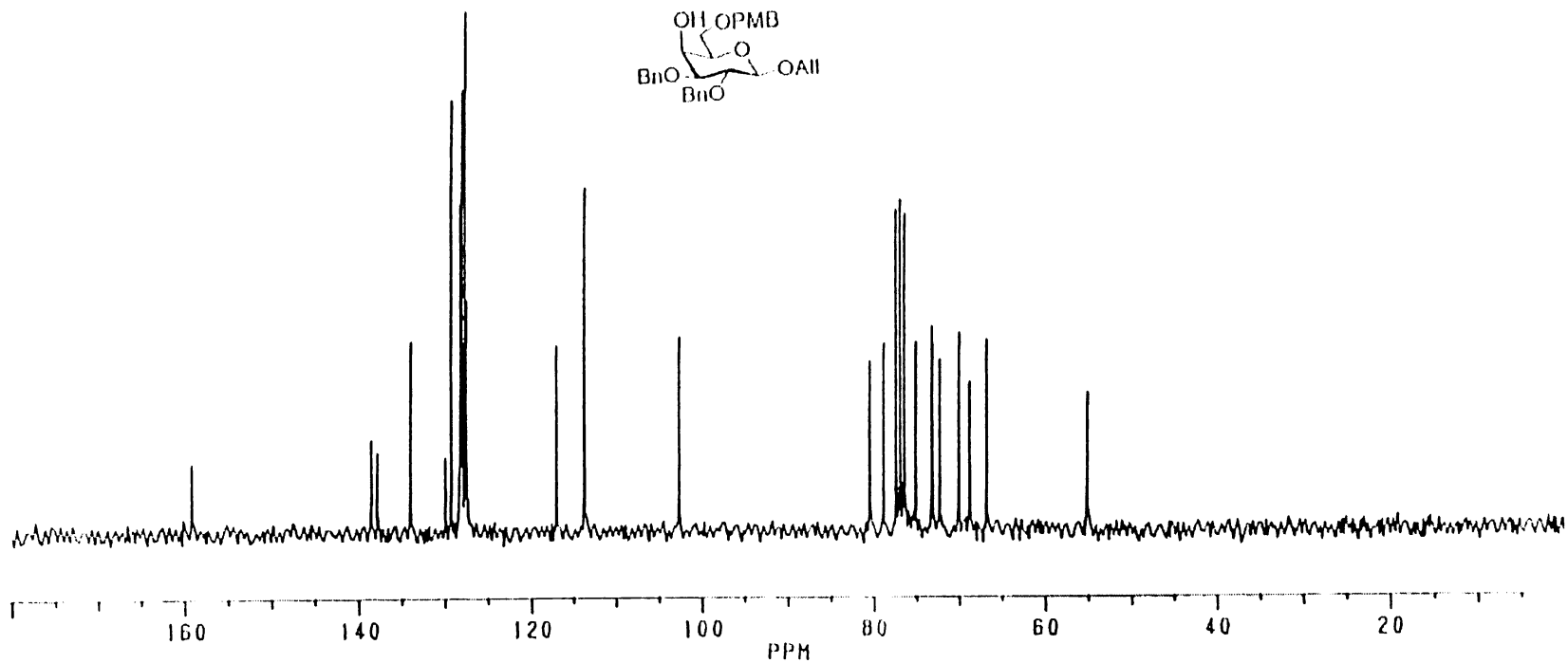
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of allyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**107**).



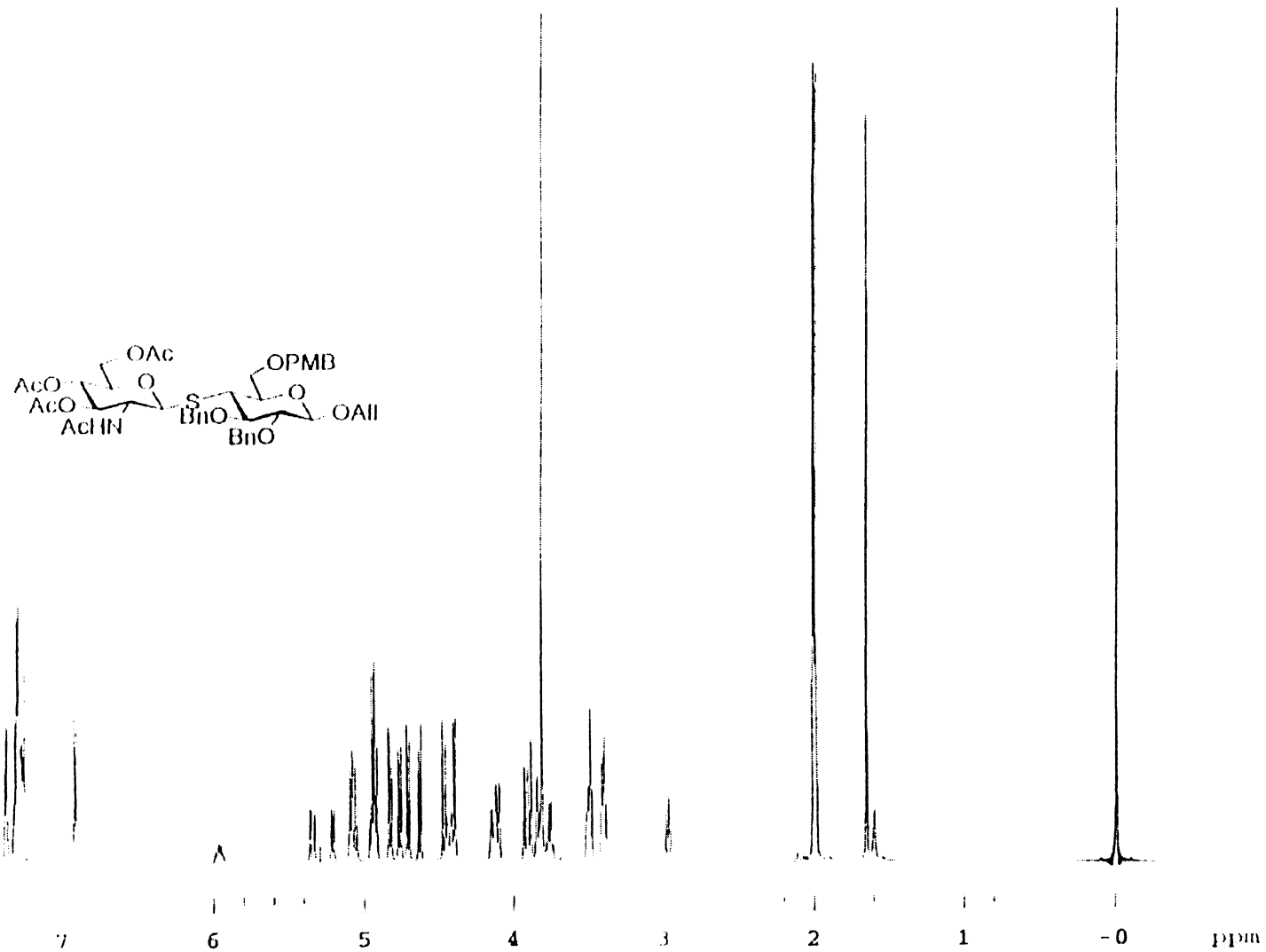
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of allyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (**107**).



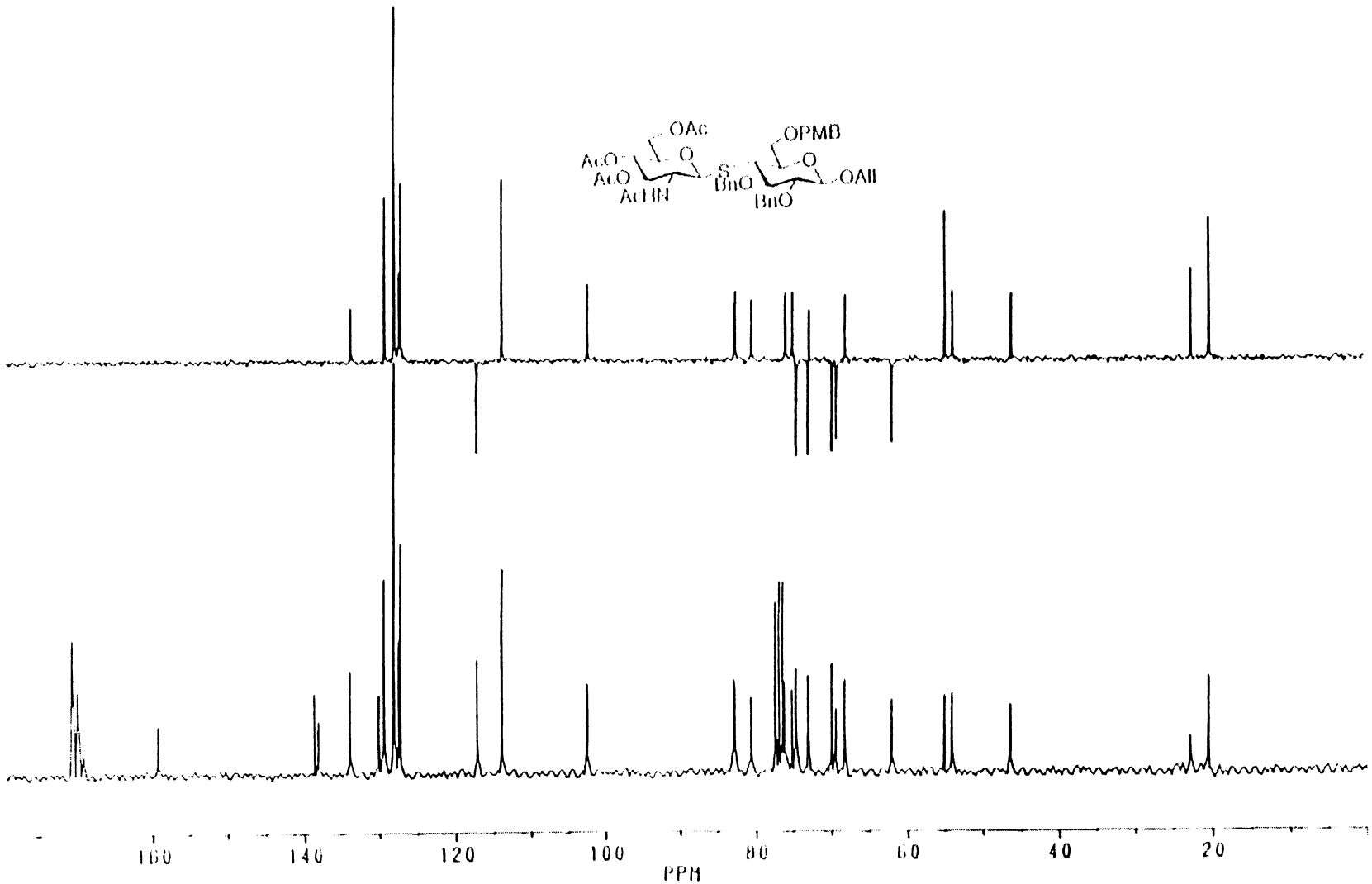
^{1}H NMR spectrum (250 MHz, $CDCl_3$) of allyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-β-D-galactopyranoside (**108**).



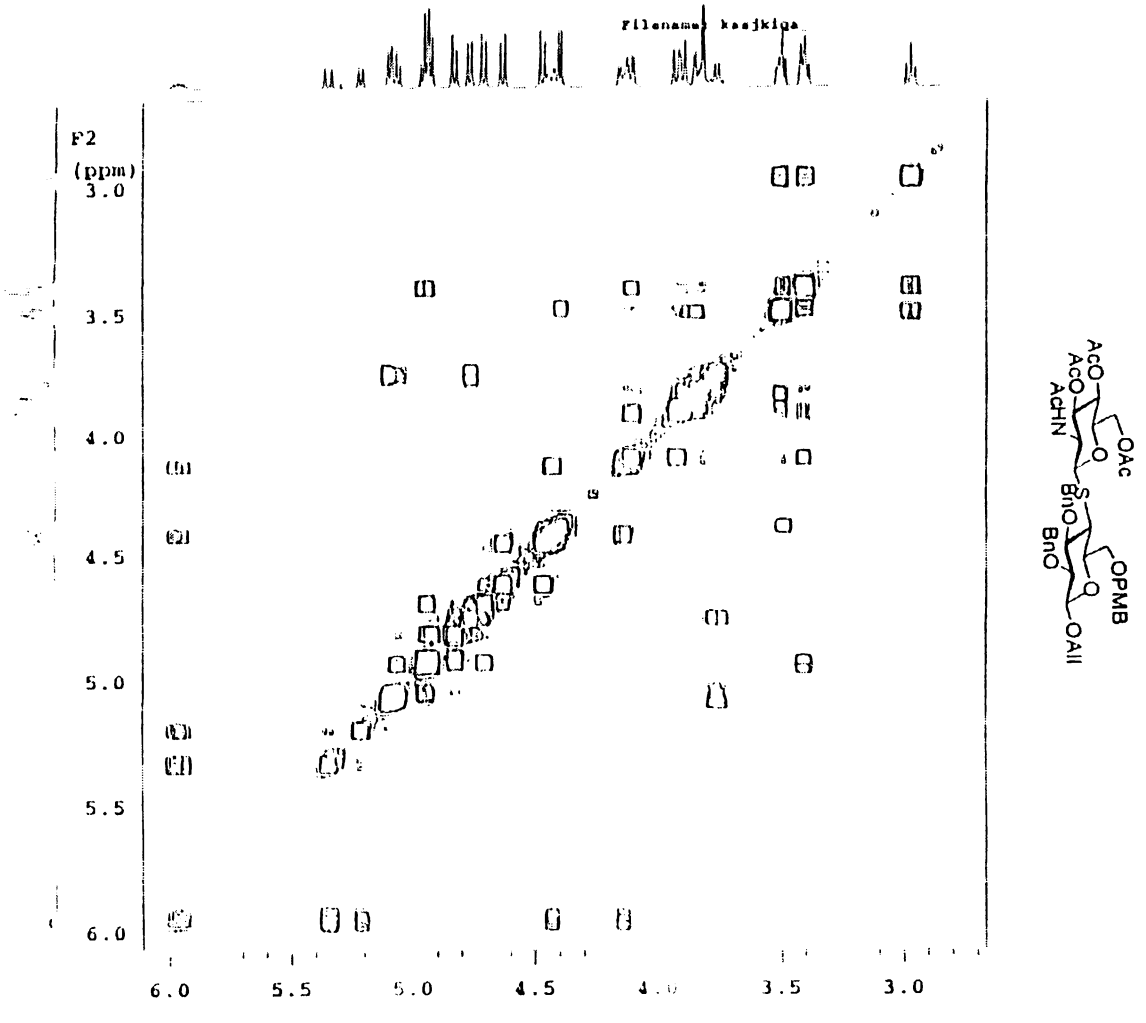
^{13}C NMR spectrum (62.5 MHz, $CDCl_3$) of allyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-*β*-D-galactopyranoside (**108**).



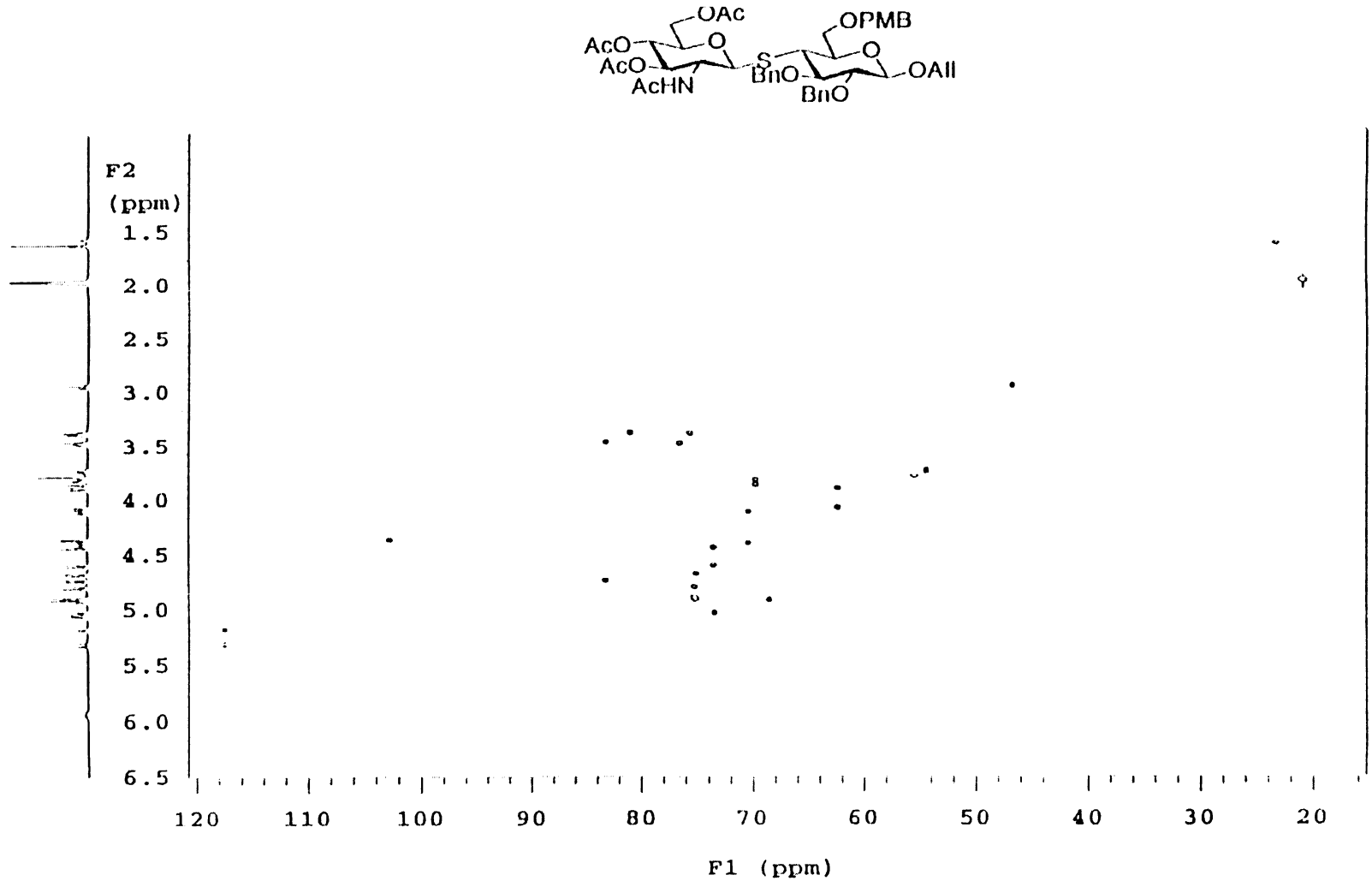
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**57**).



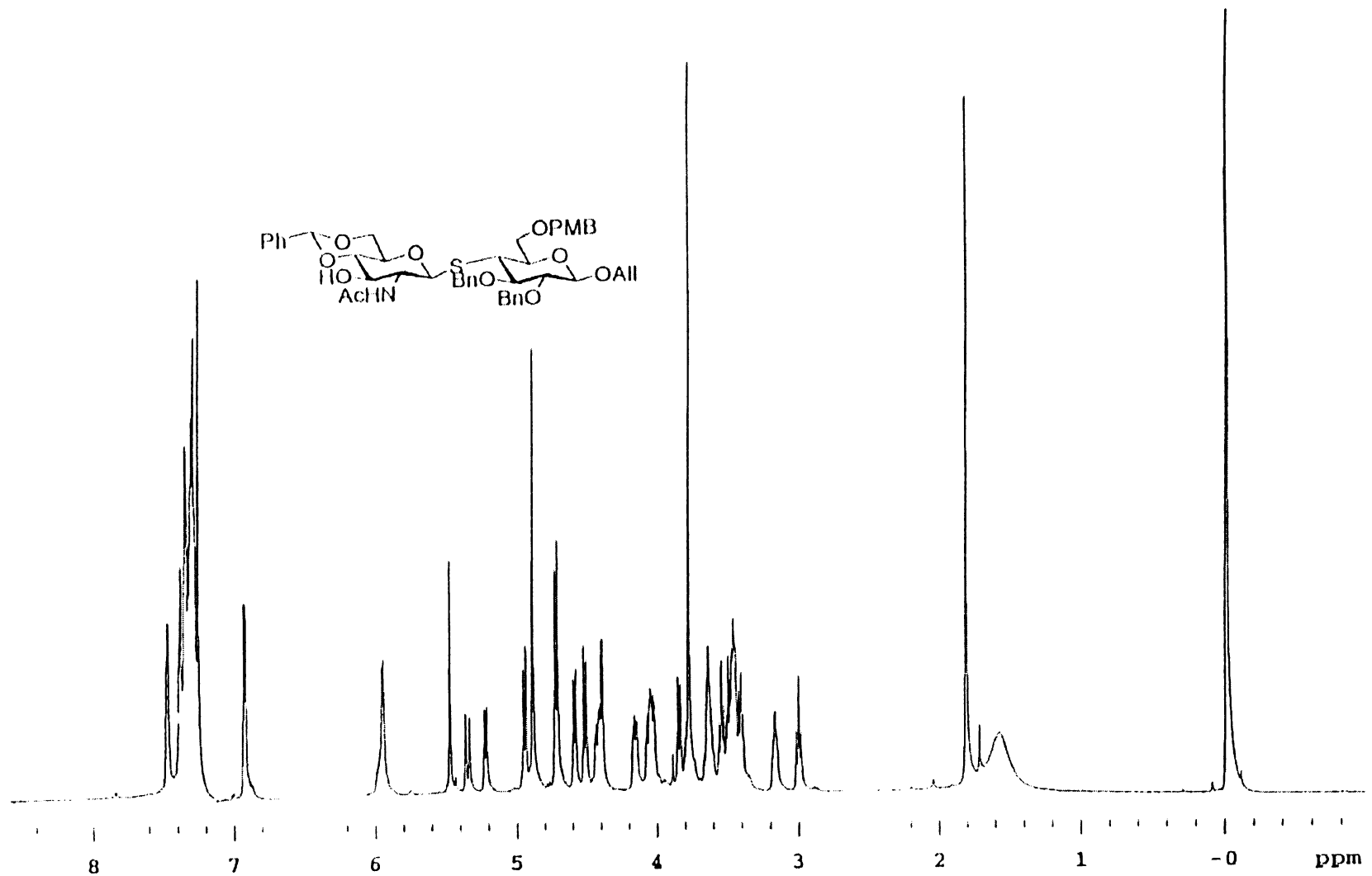
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**57**).



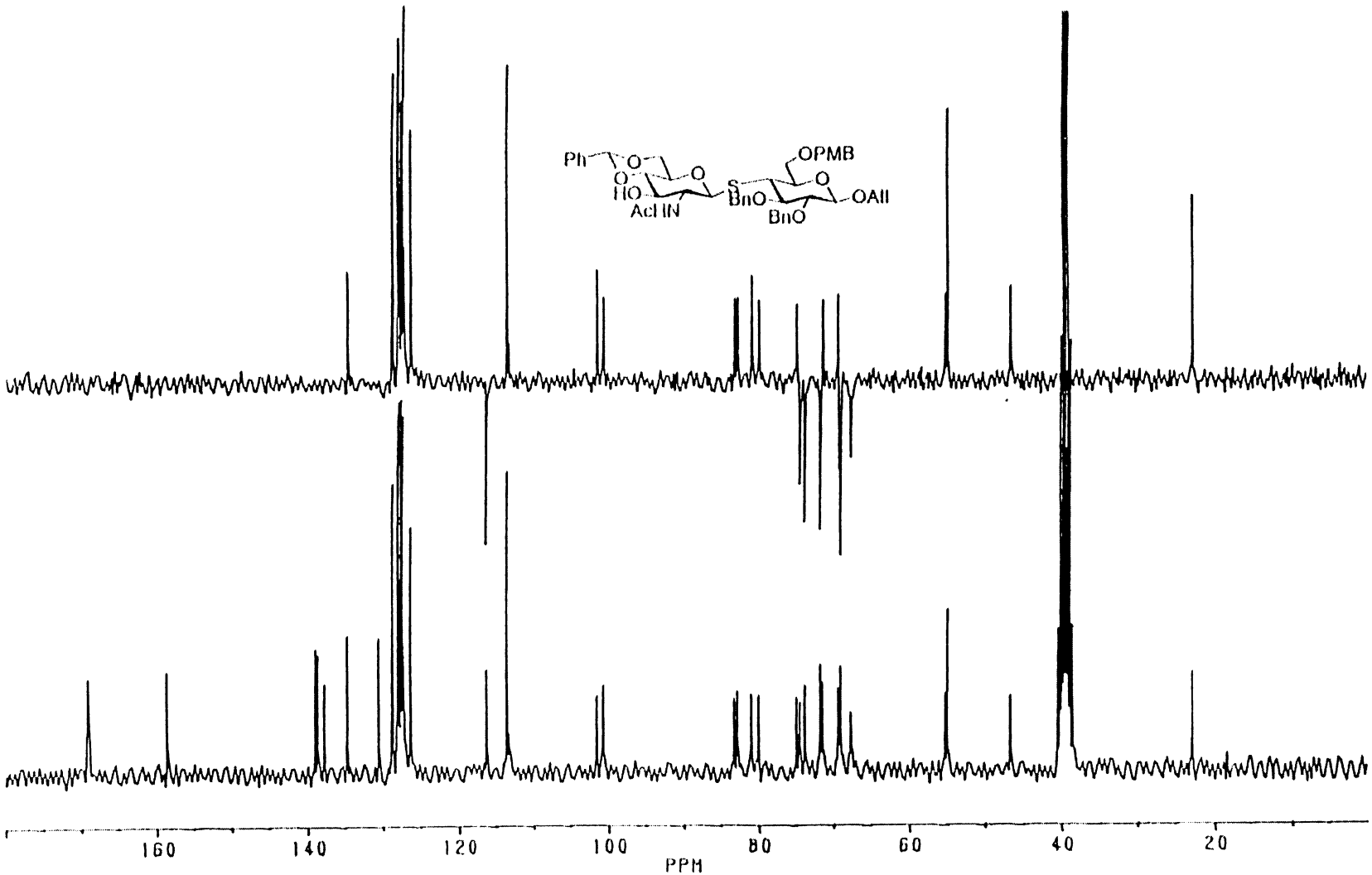
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**57**).



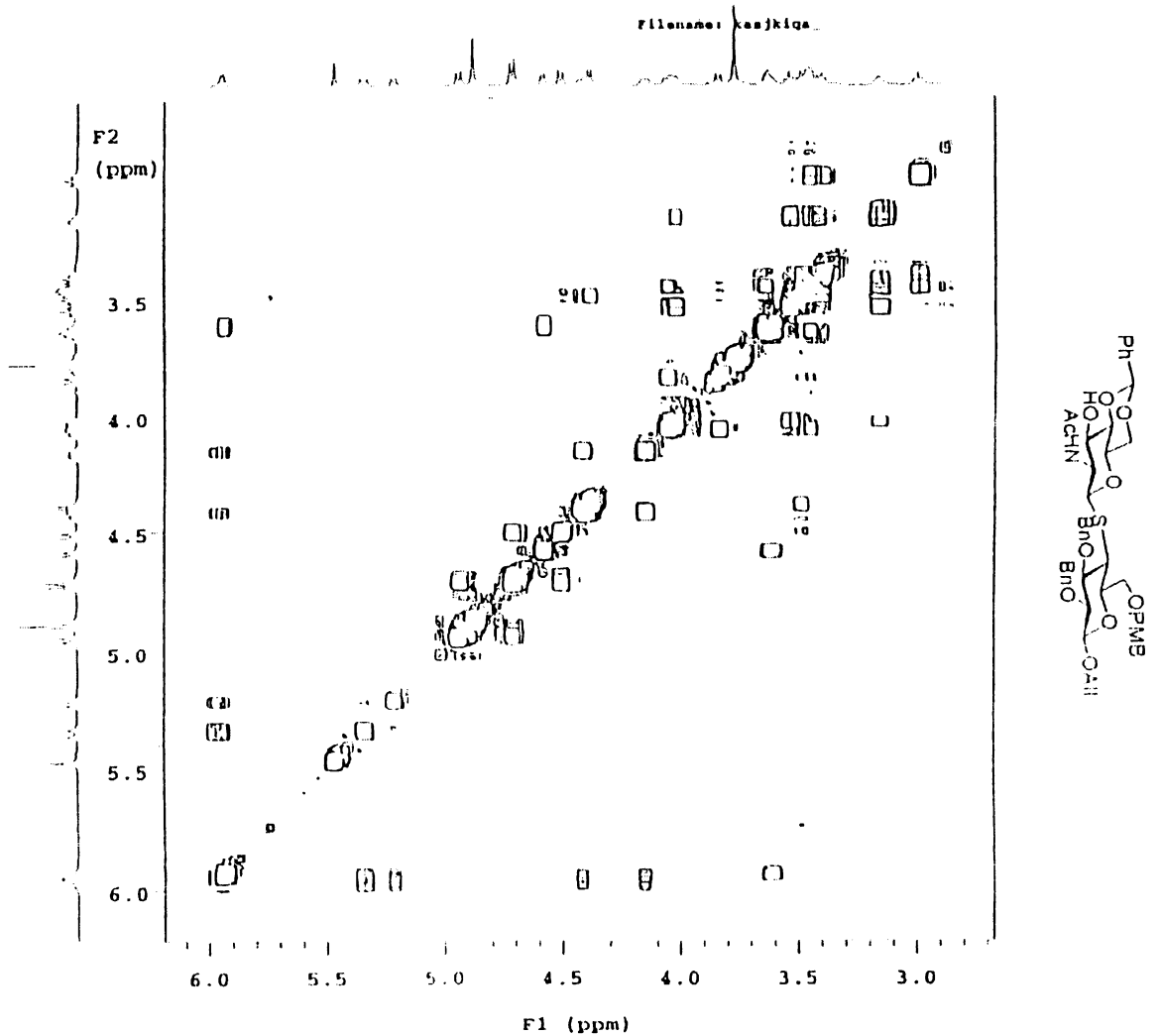
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**57**).



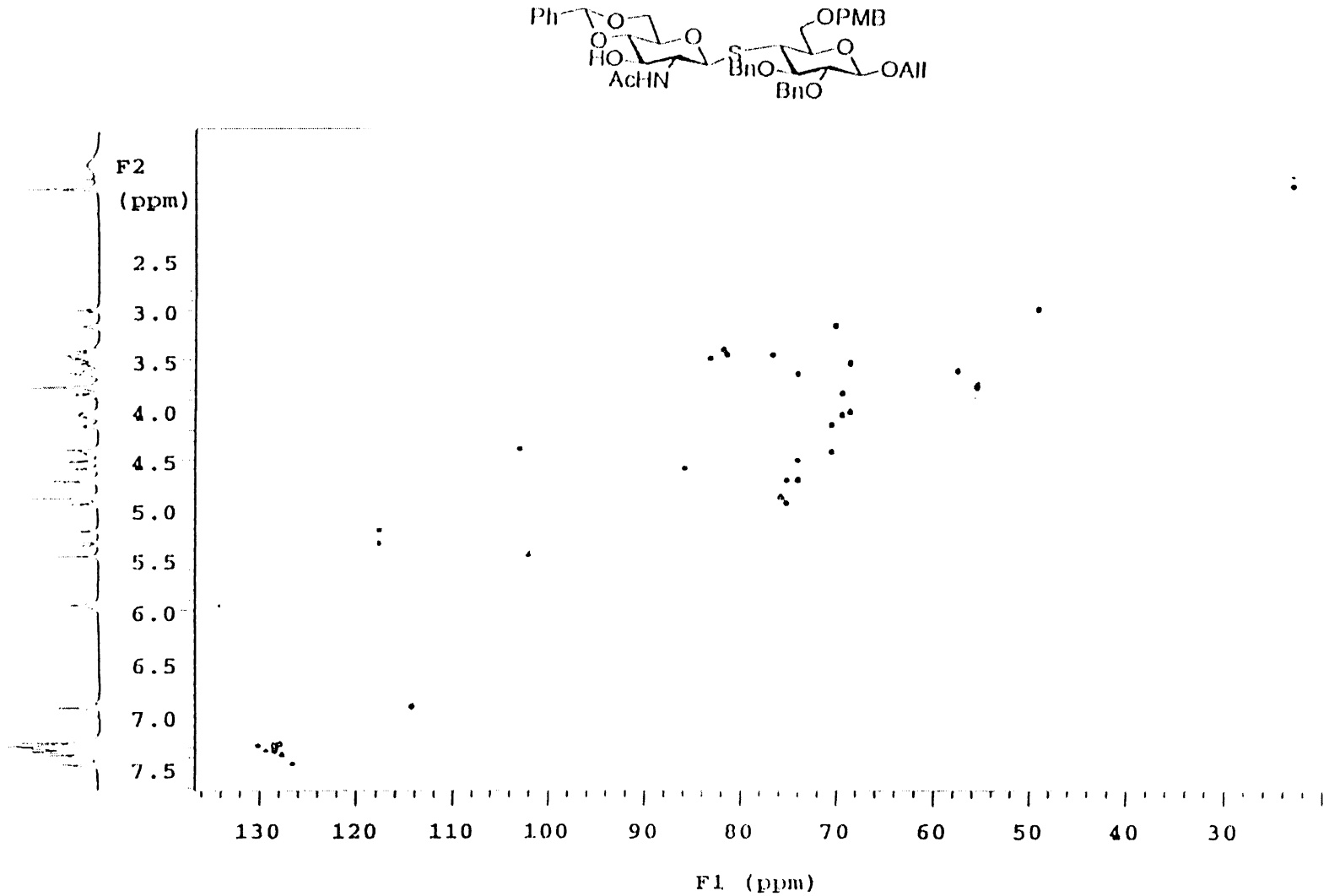
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**55**).



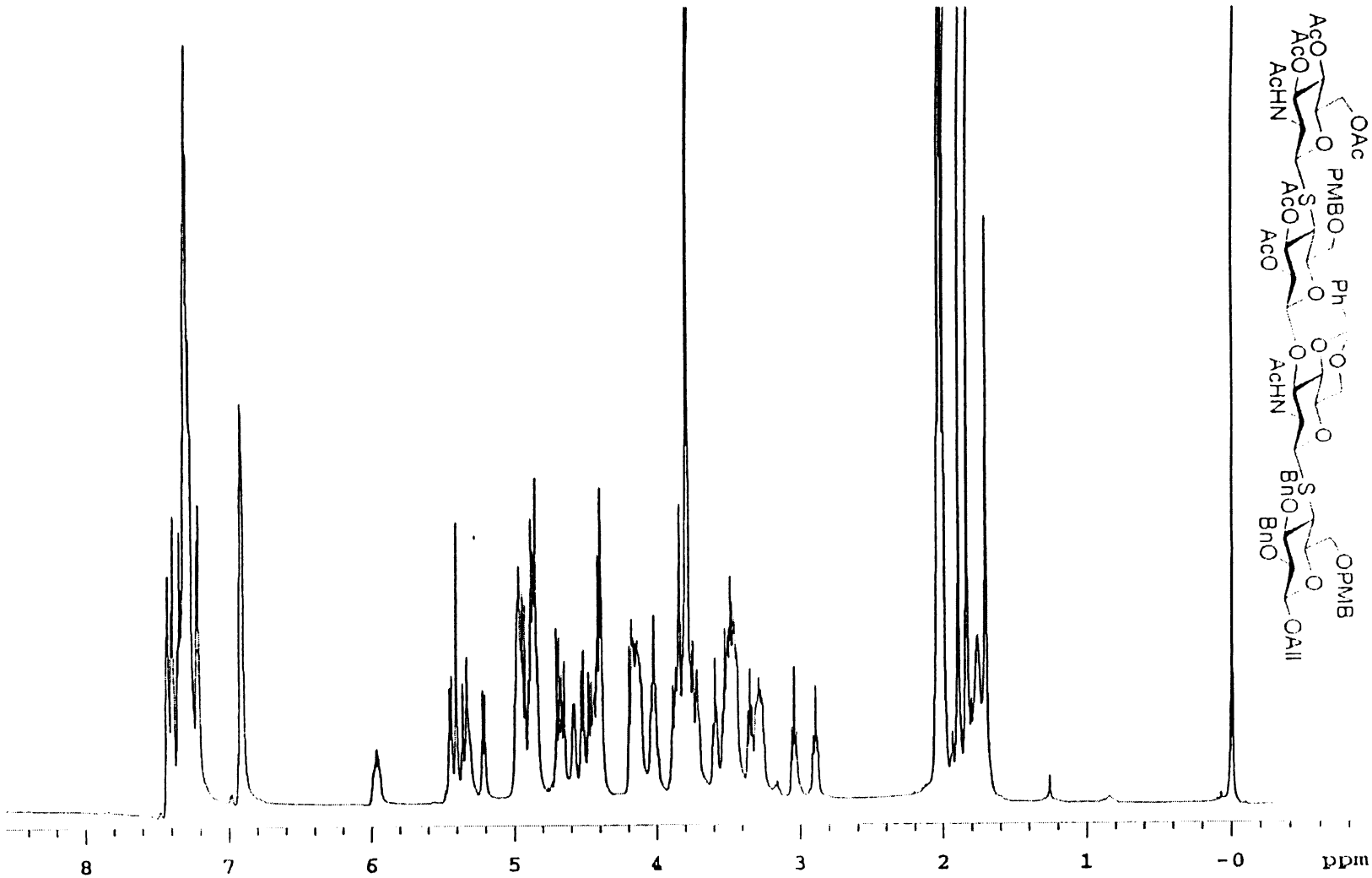
^{13}C NMR and DEPT spectra (62.5 MHz, DMSO-d_6) of allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**55**).



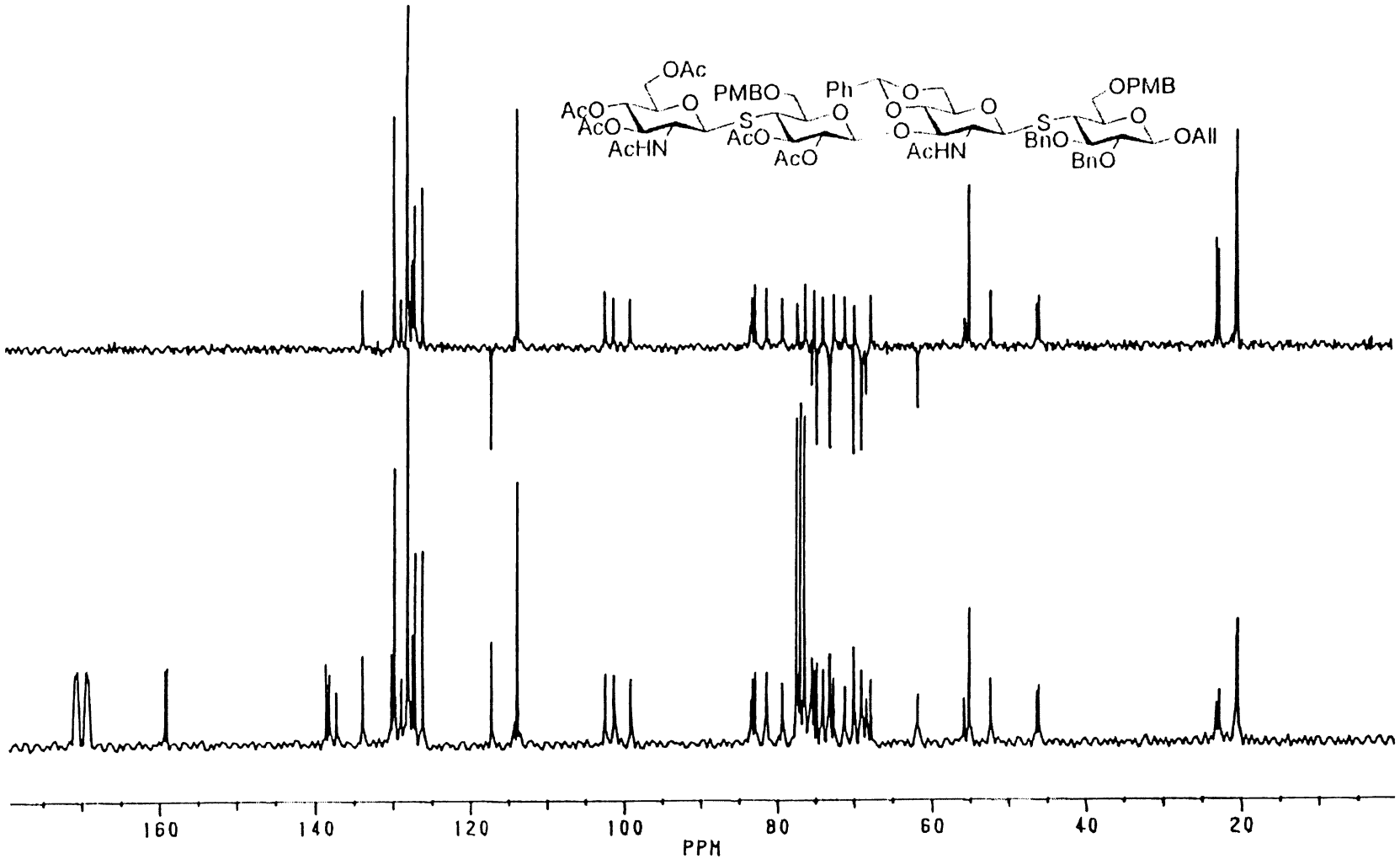
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**55**).



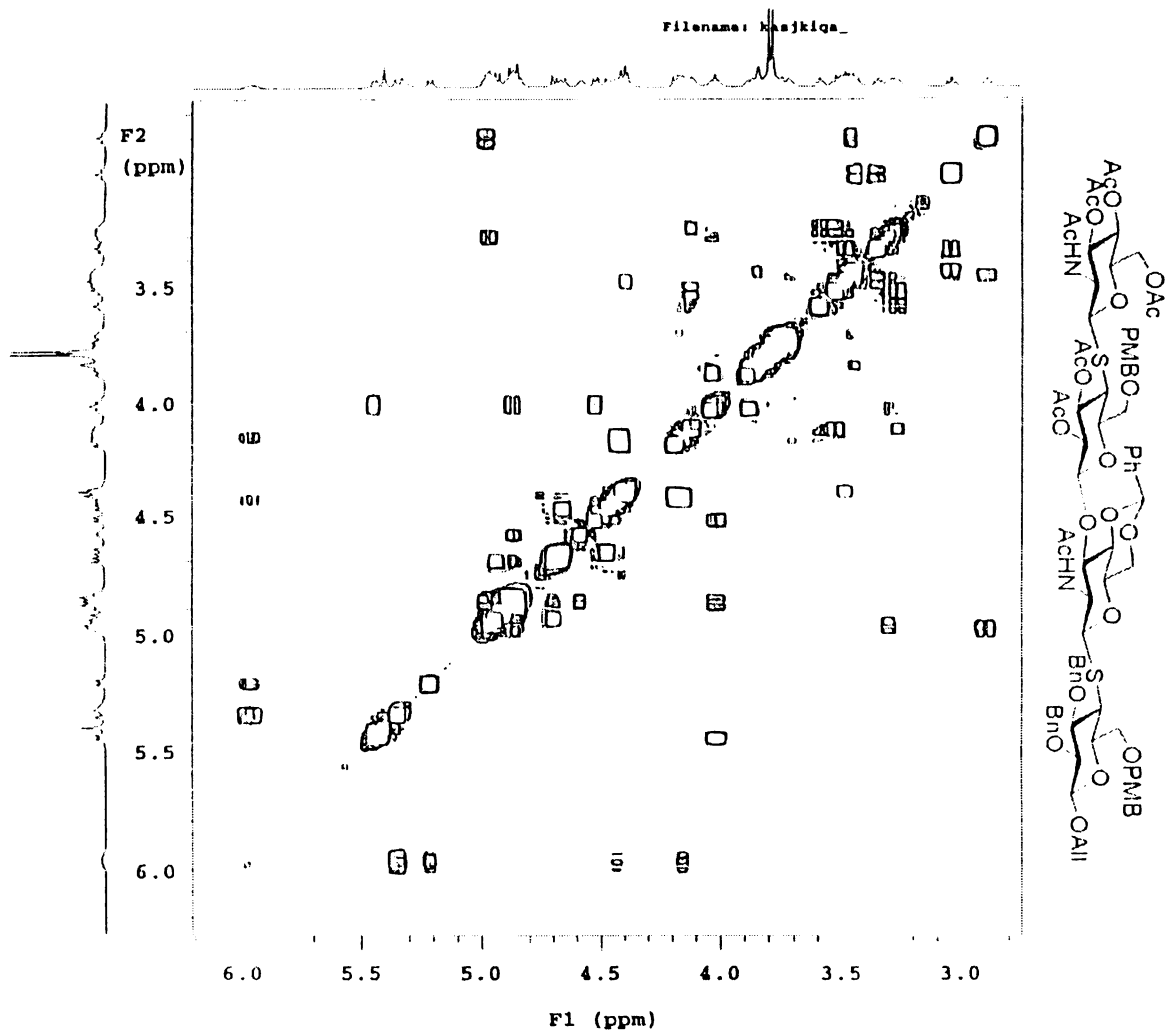
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**55**).



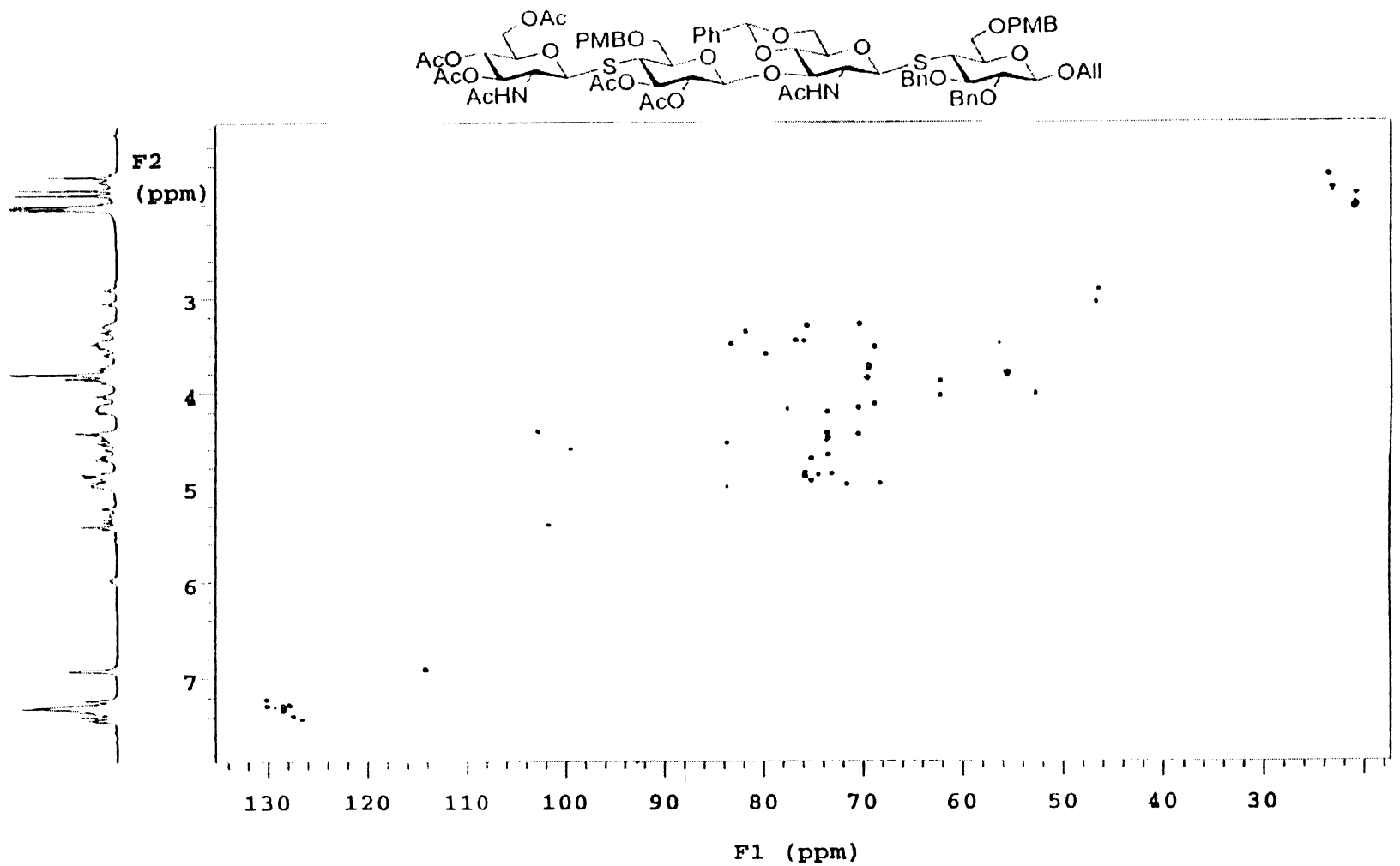
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**53**).



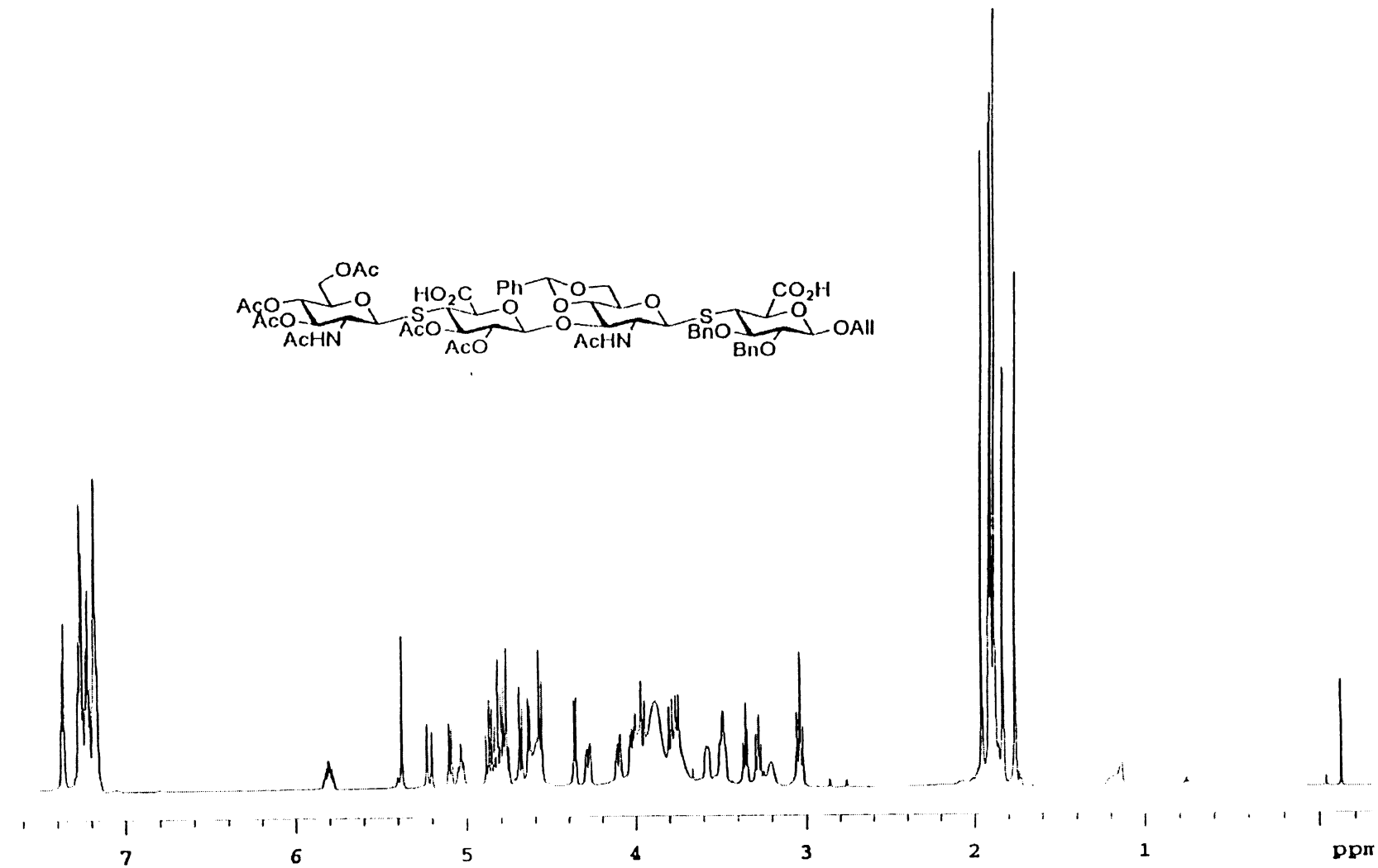
^{13}C NMR and DEPT spectra (62.5 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**53**).



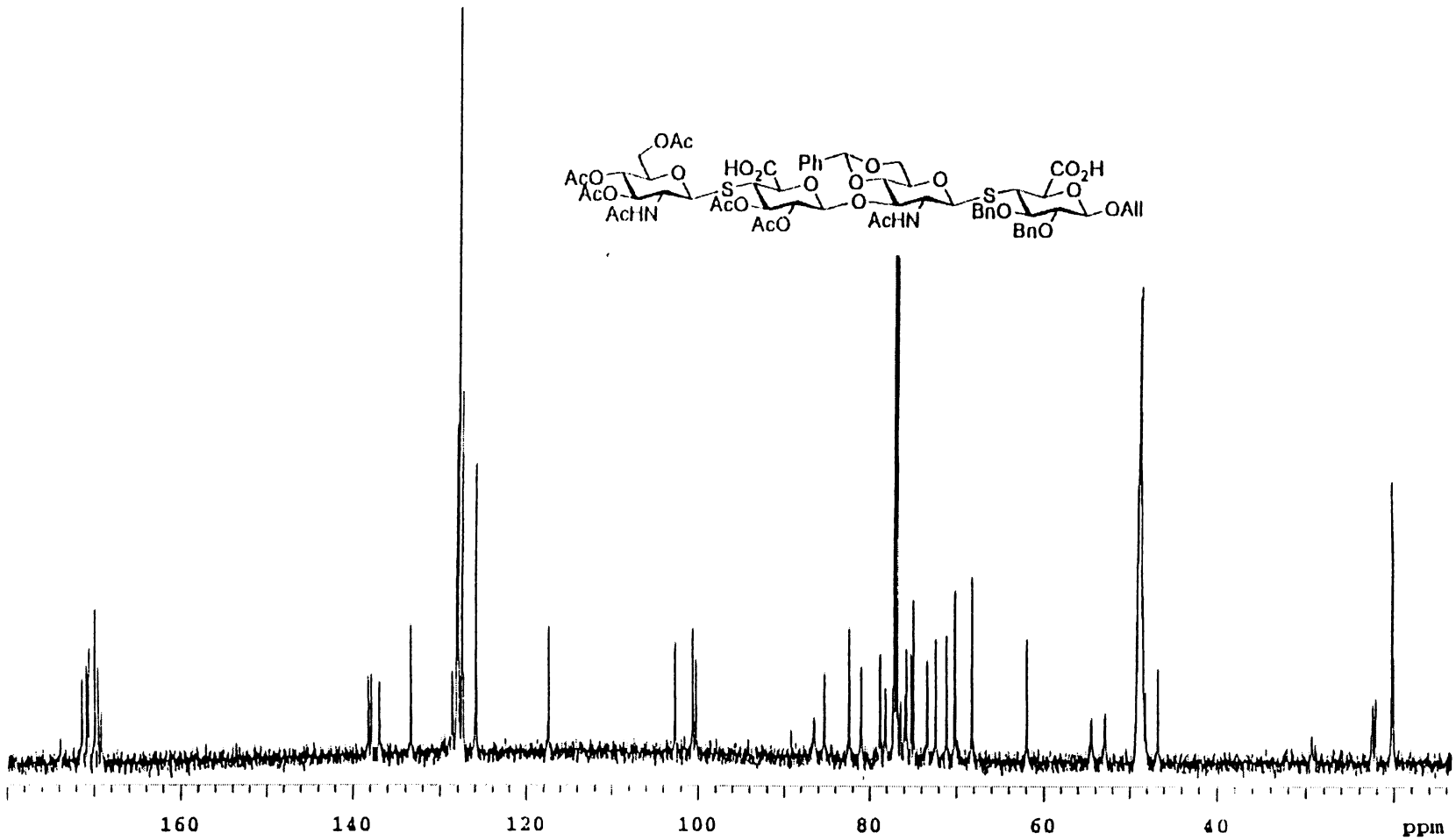
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**53**).



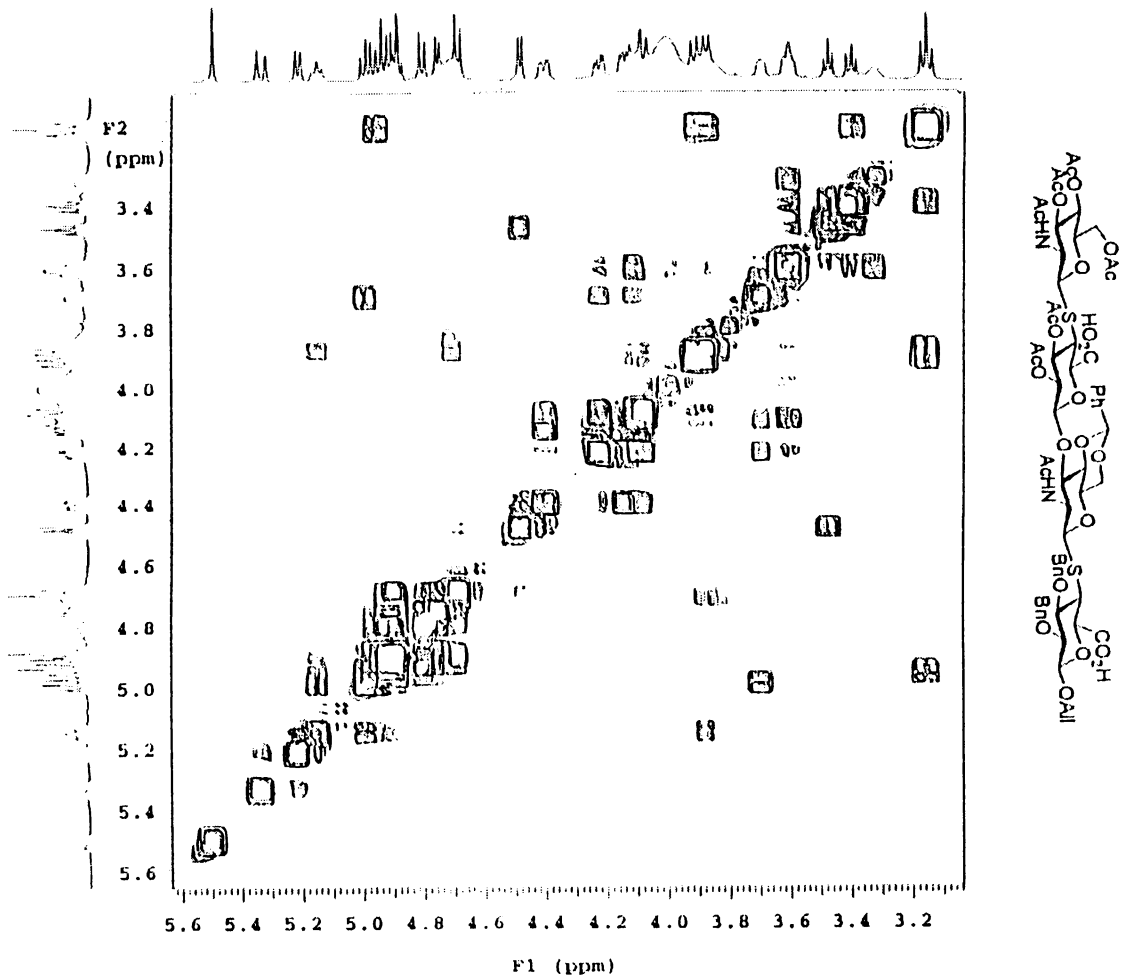
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**53**).



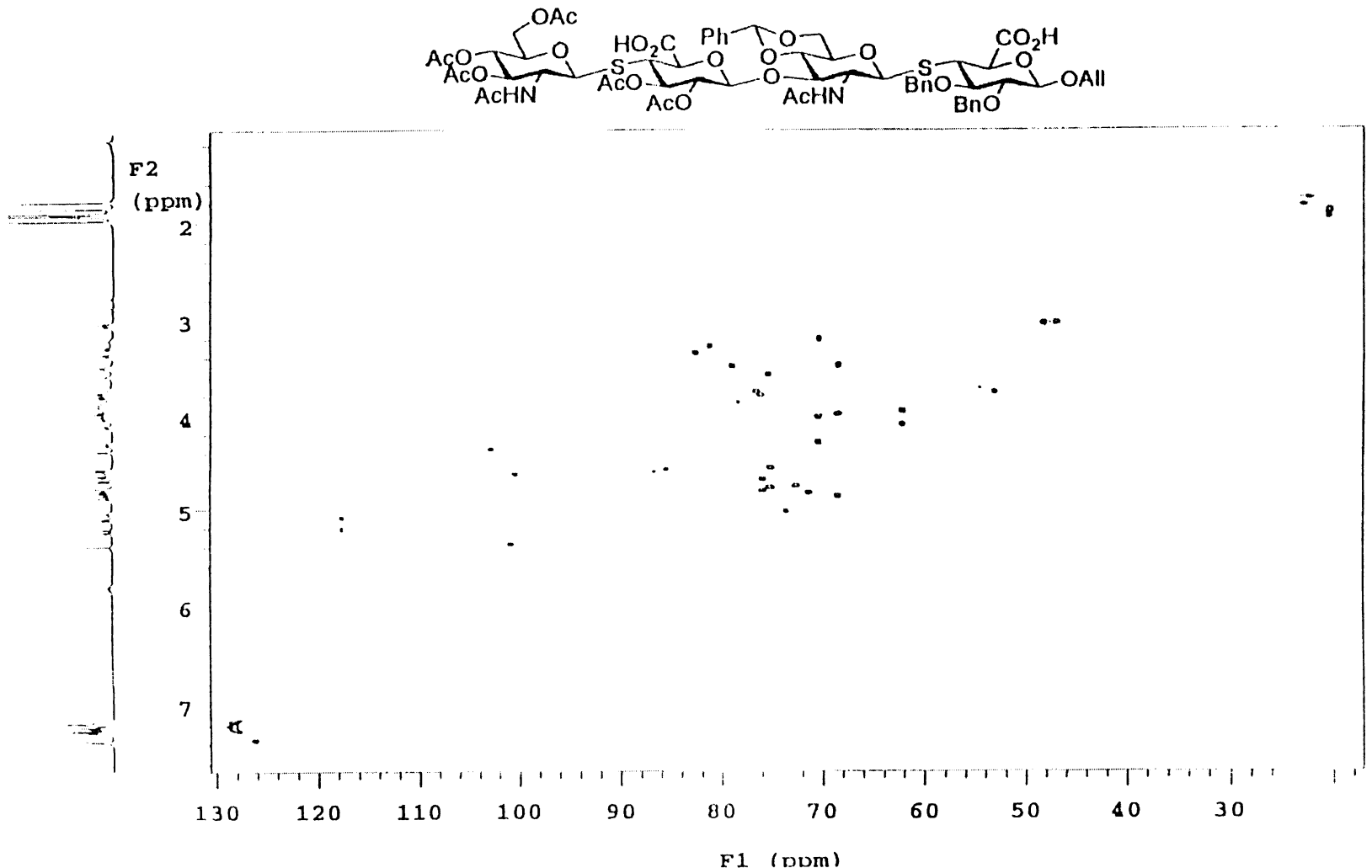
^{1}H NMR spectrum (600 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-4-thio-*β*-D-glucopyranosiduronic acid **(110)**.



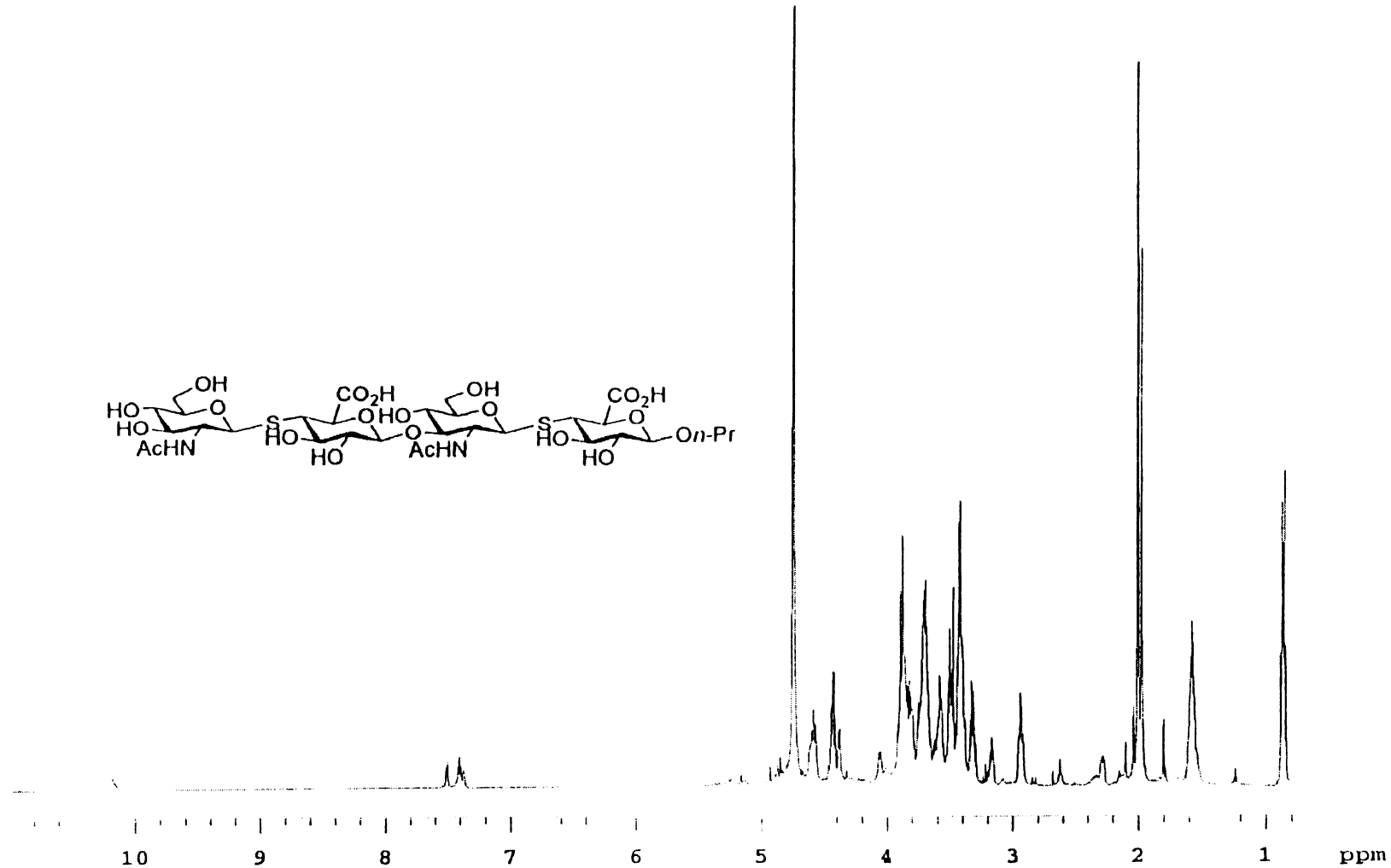
^{13}C NMR spectrum (75 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-4-thio-*β*-D-glucopyranosiduronic acid (**110**).



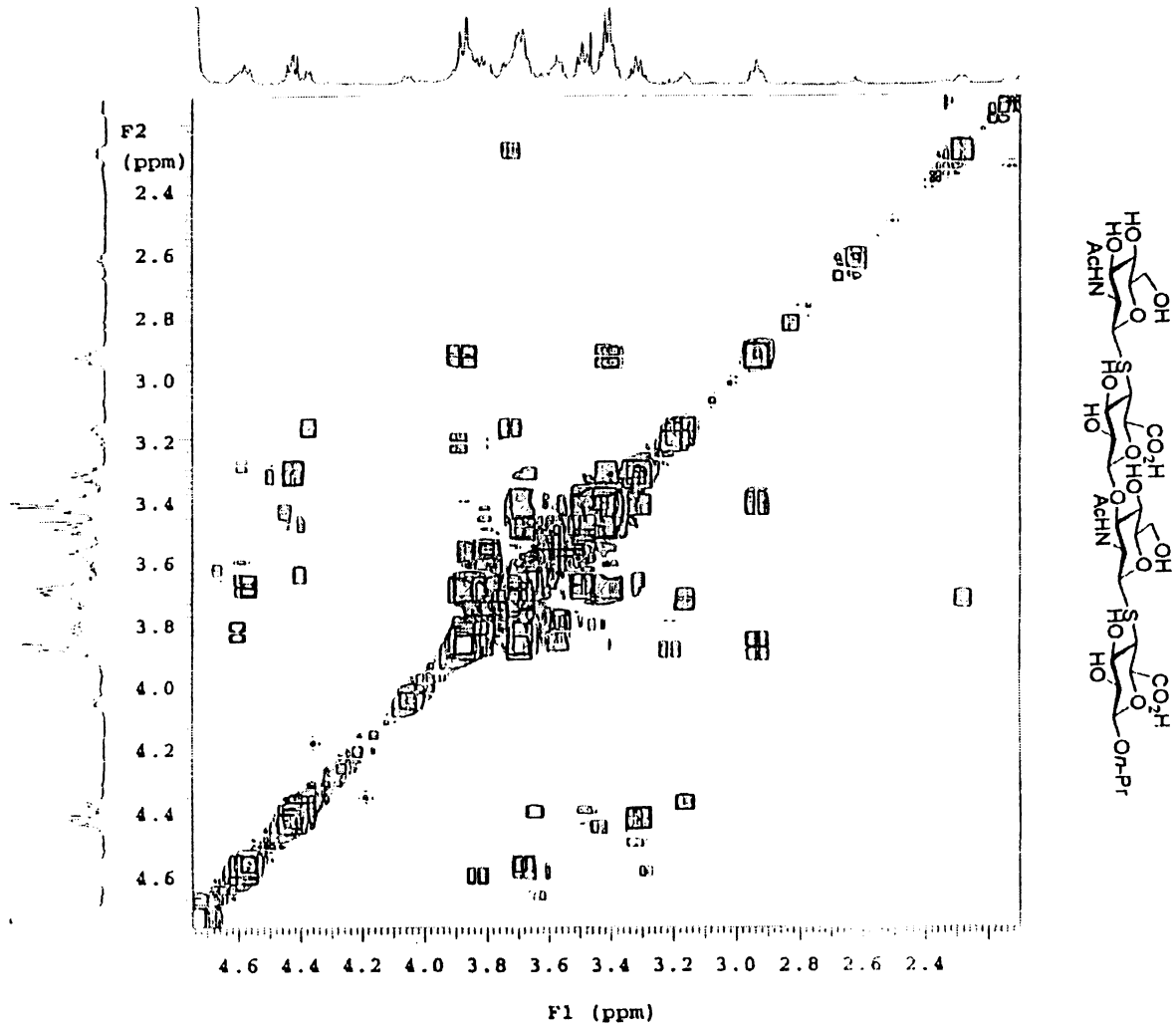
gCOSY spectrum (600 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-4-thio-*β*-D-glucopyranosiduronic acid **(110)**.



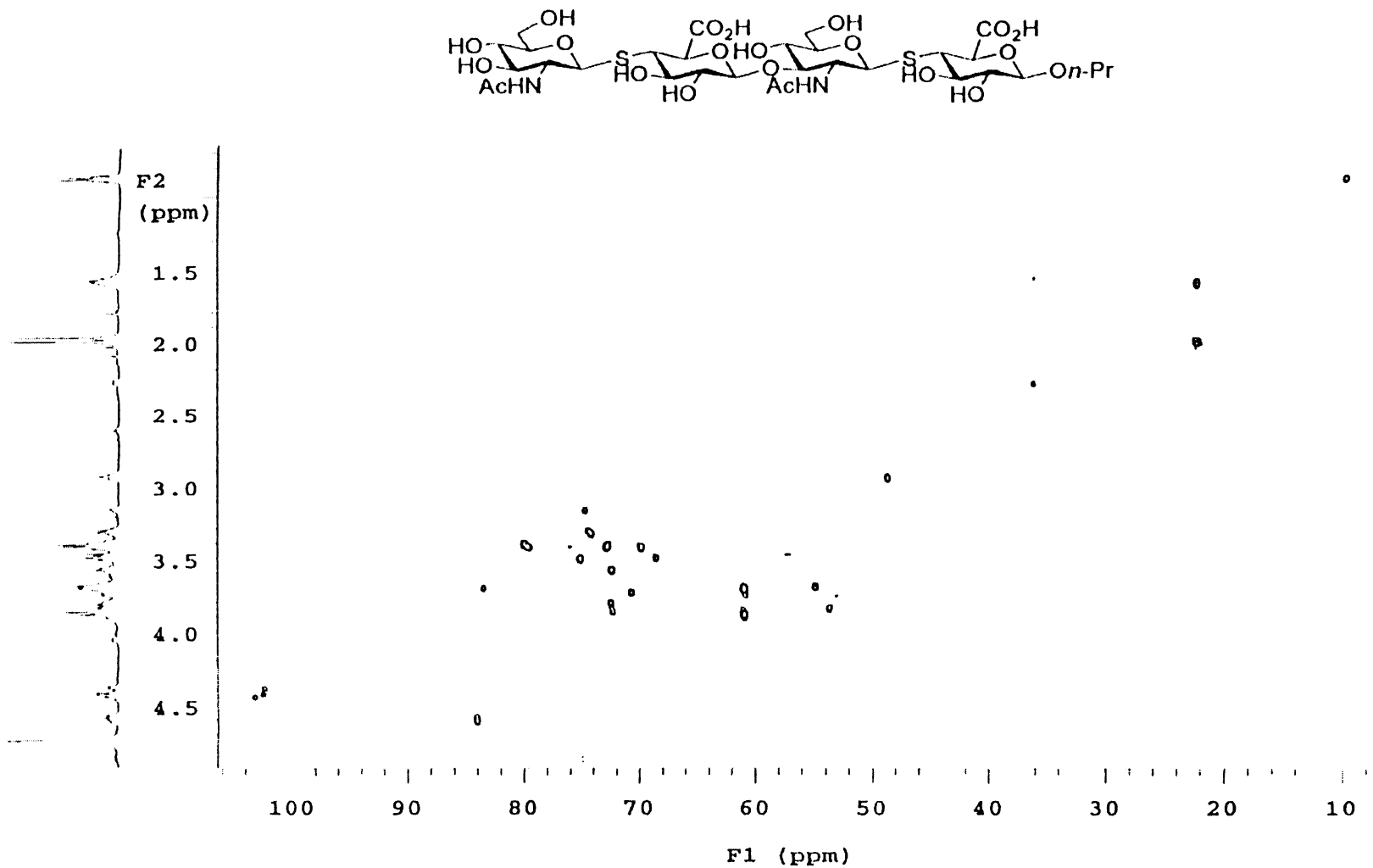
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-4-thio-*β*-D-glucopyranosiduronic acid (**110**).



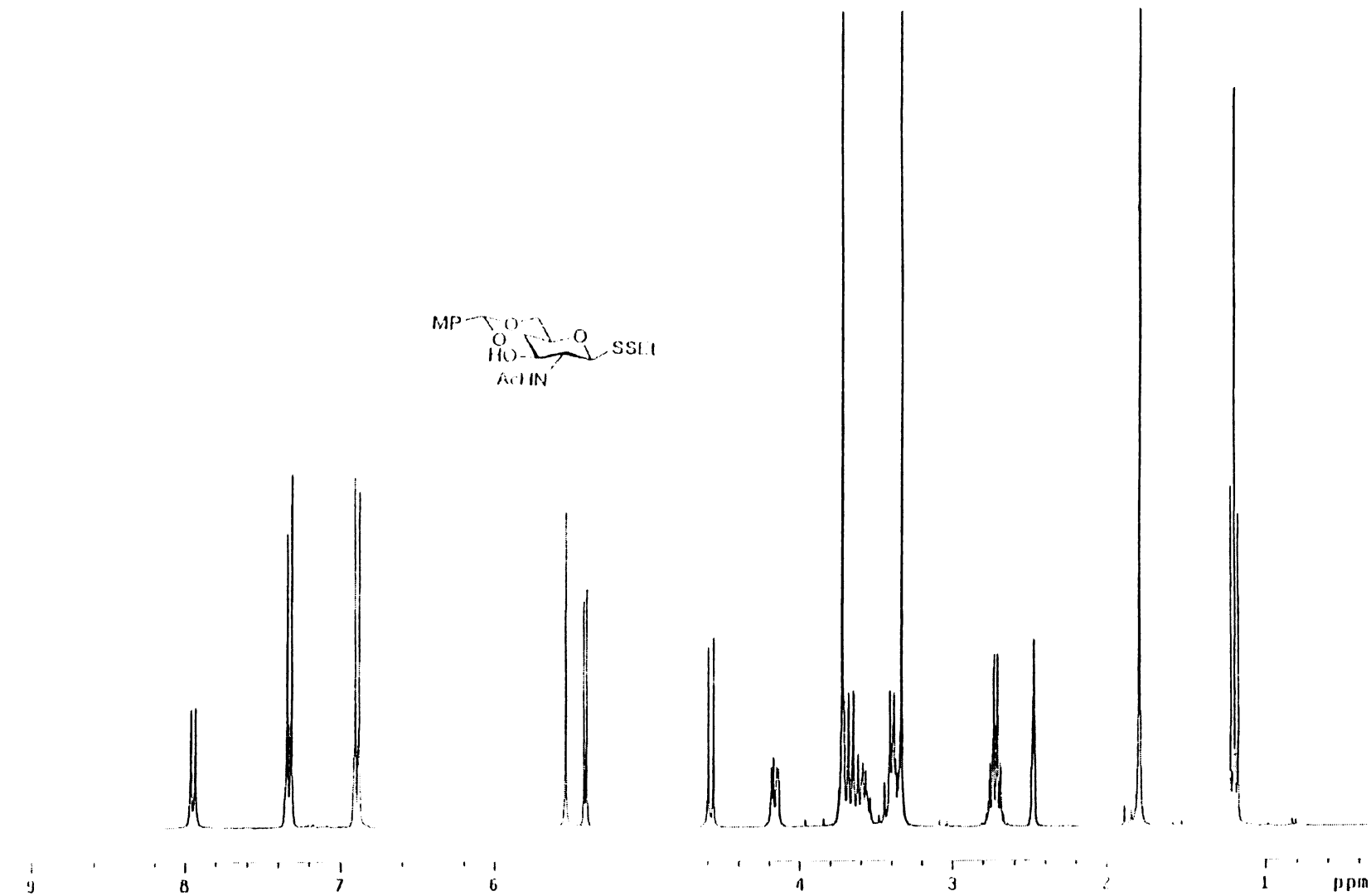
^{1}H NMR spectrum (600 MHz, D_2O) of *n*-propyl *S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-4-thio-*β*-D-glucopyranosiduronic acid (**52**).



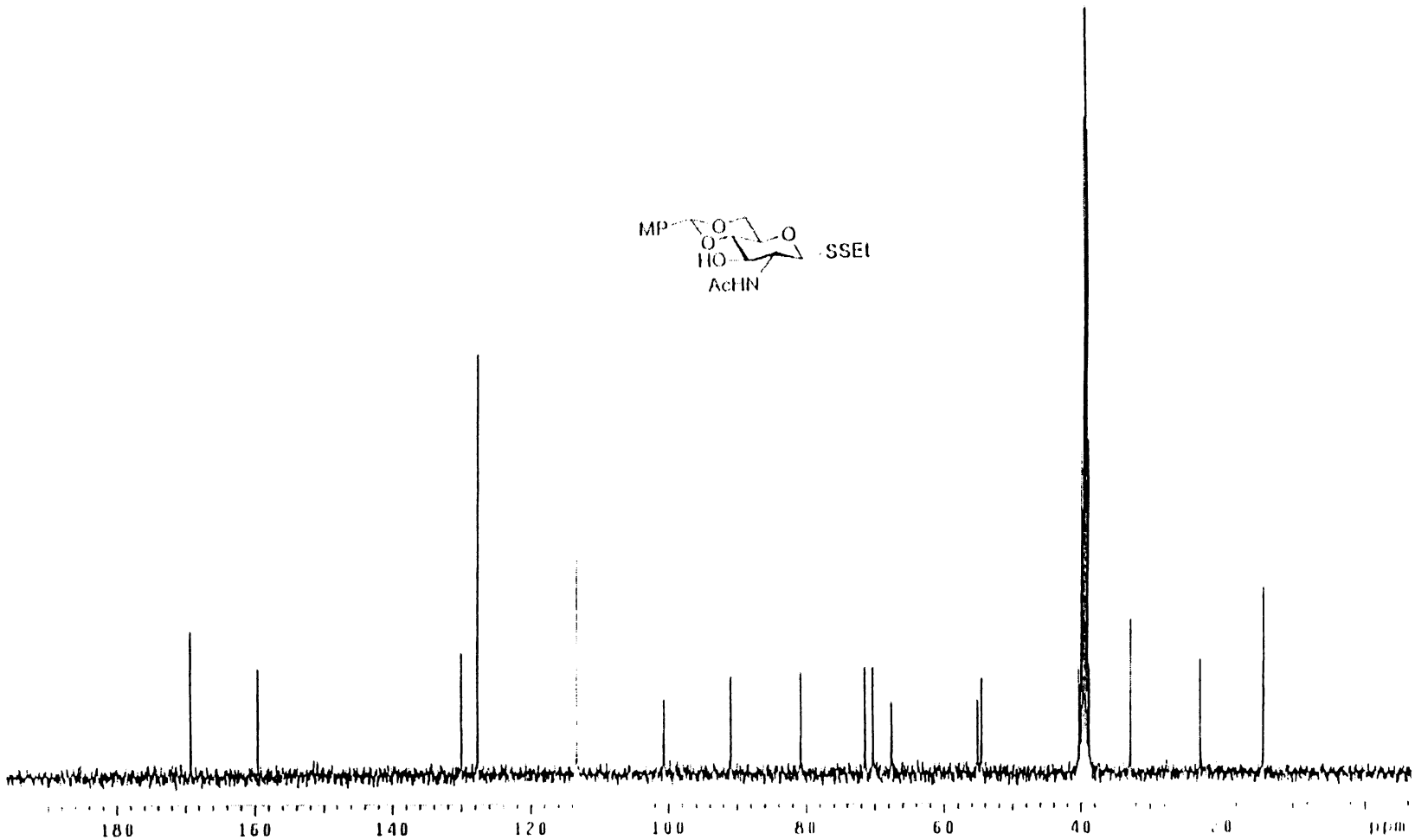
gCOSY spectrum (600 MHz, D_2O) of *n*-propyl *S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-4-thio-*β*-D-glucopyranosiduronic acid (**52**).



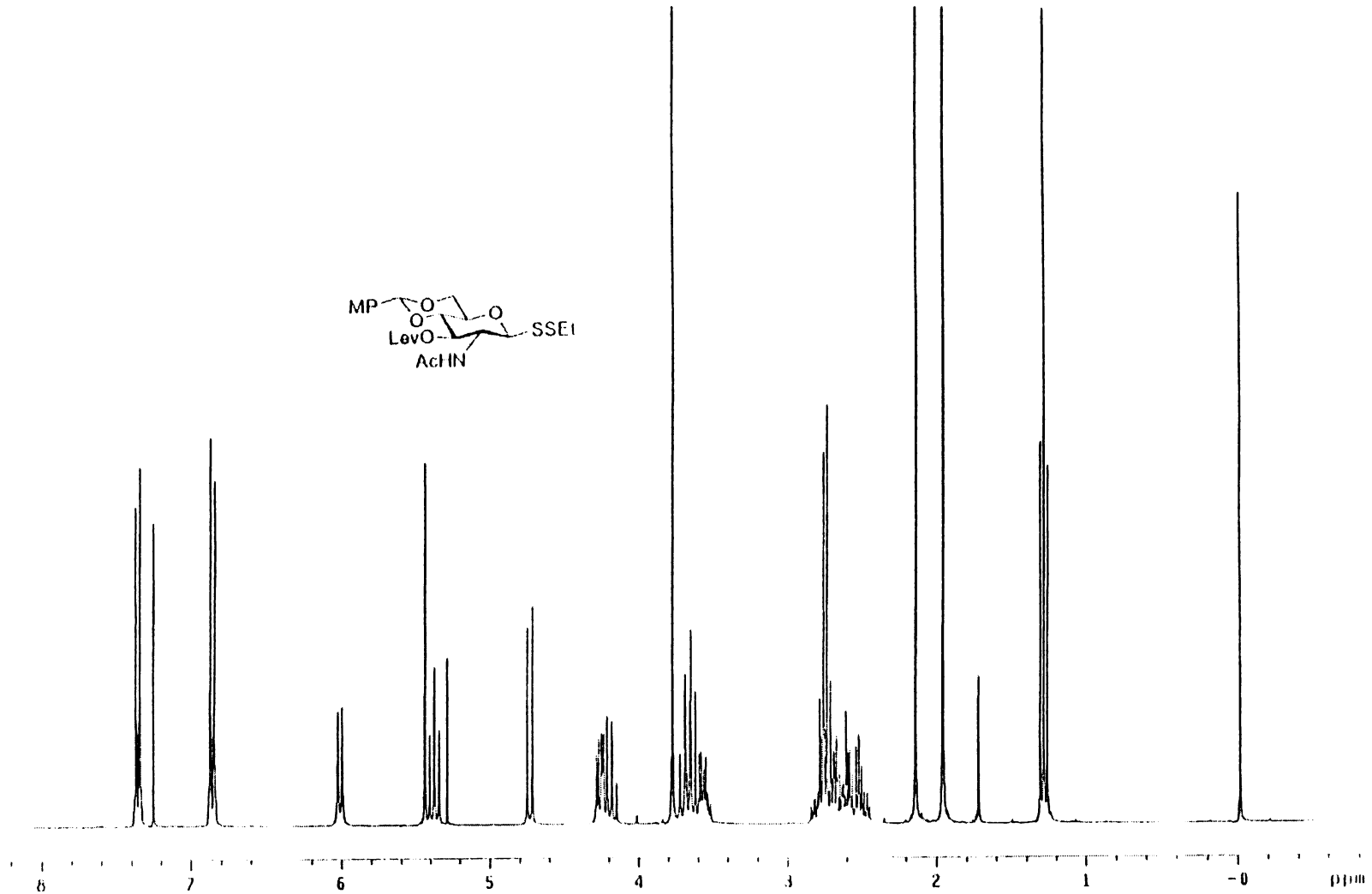
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, D_2O) of *n*-propyl *S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-4-thio-*β*-D-glucopyranosiduronic acid (**52**).



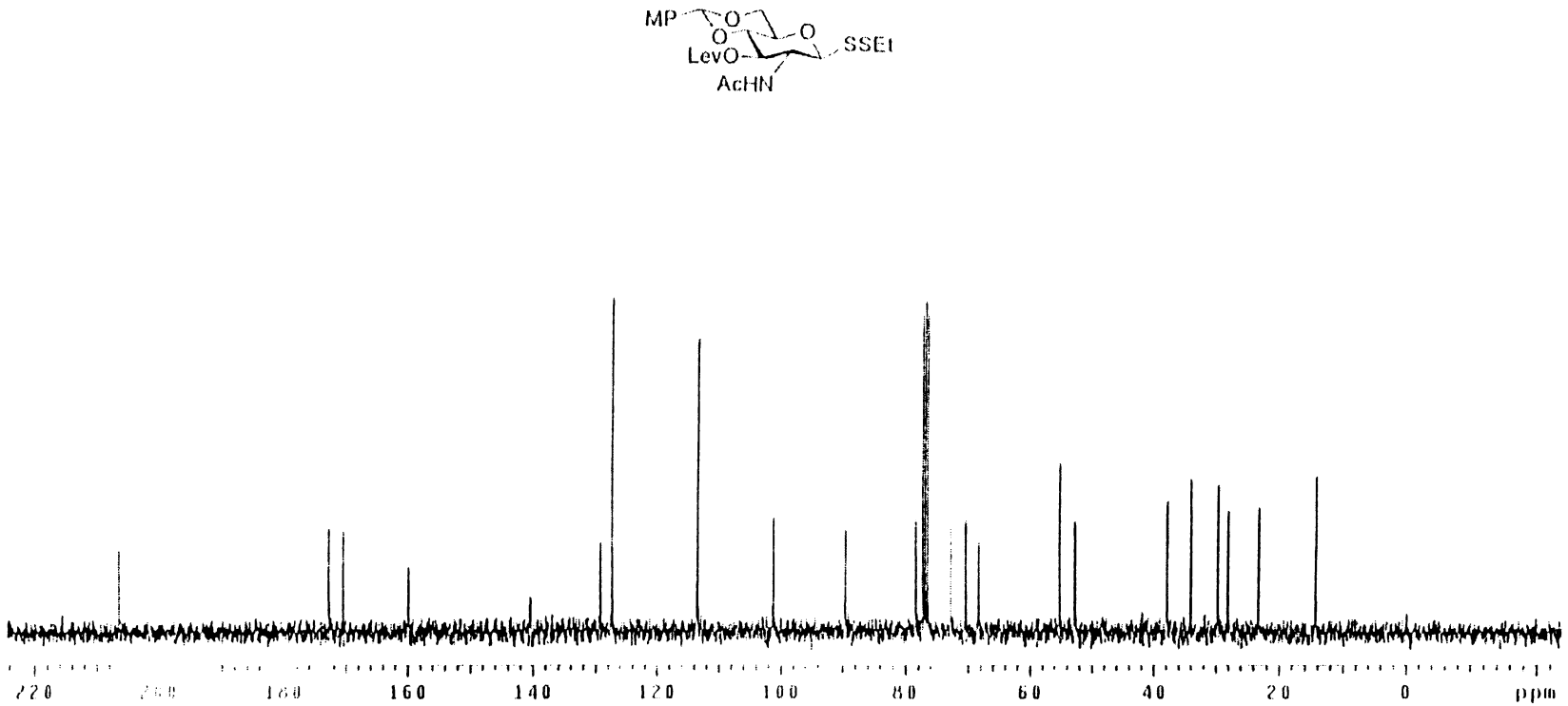
^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-acetamido-1,2-dideoxy-1-ethyldithio-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (**123**).



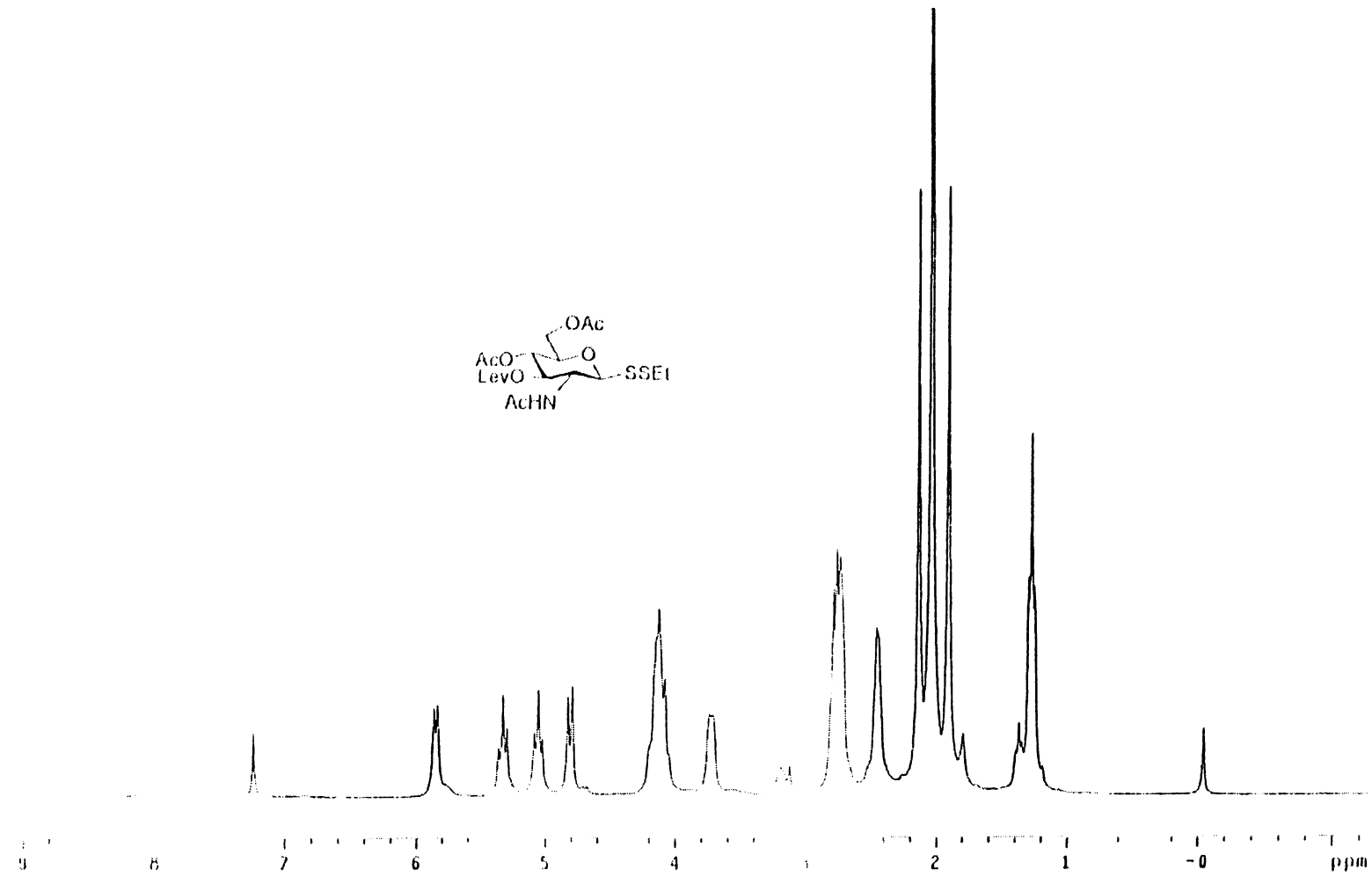
^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-acetamido-1,2-dideoxy-1-ethyldithio-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (**123**).



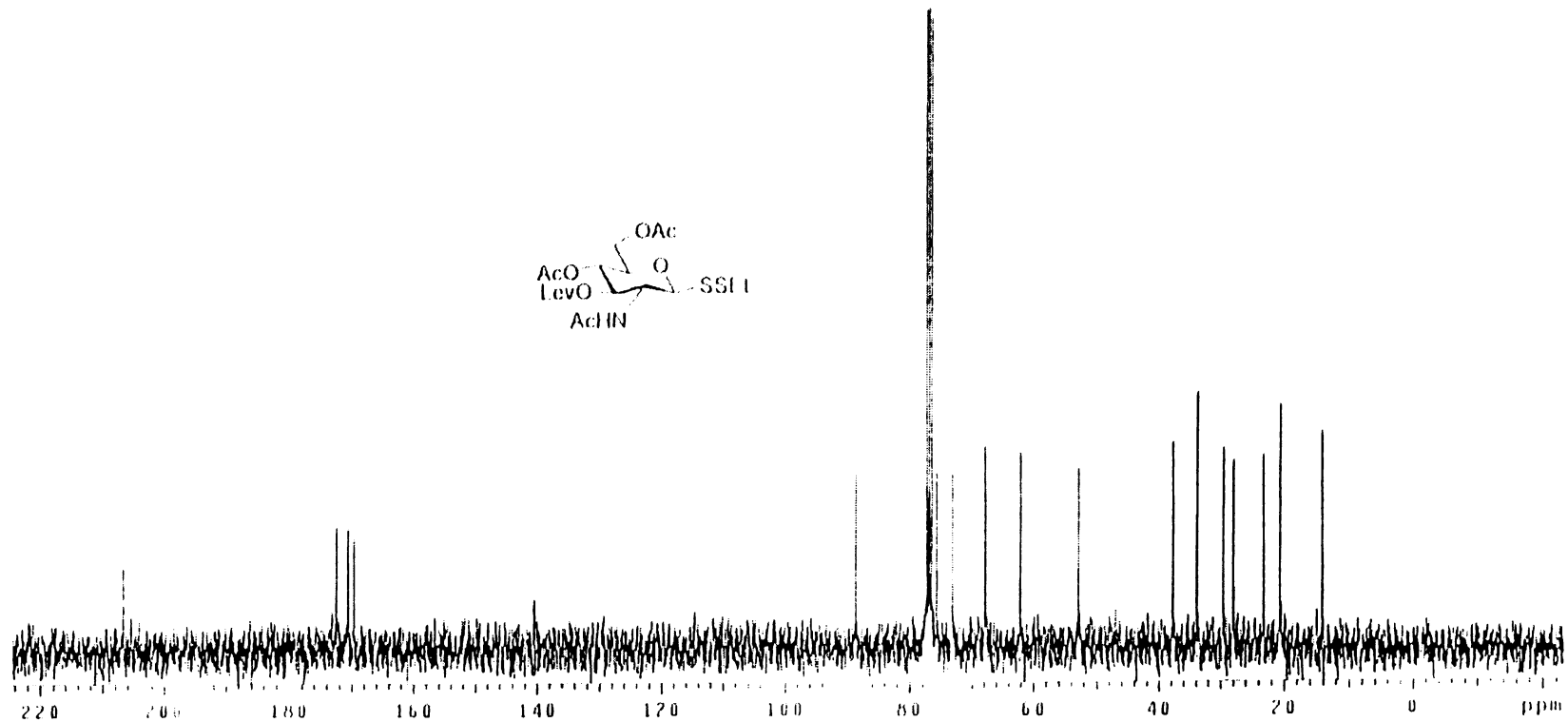
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2-acetamido-1,2-dideoxy-1-ethyldithio-3-*O*-levulinoyl-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (**124**).



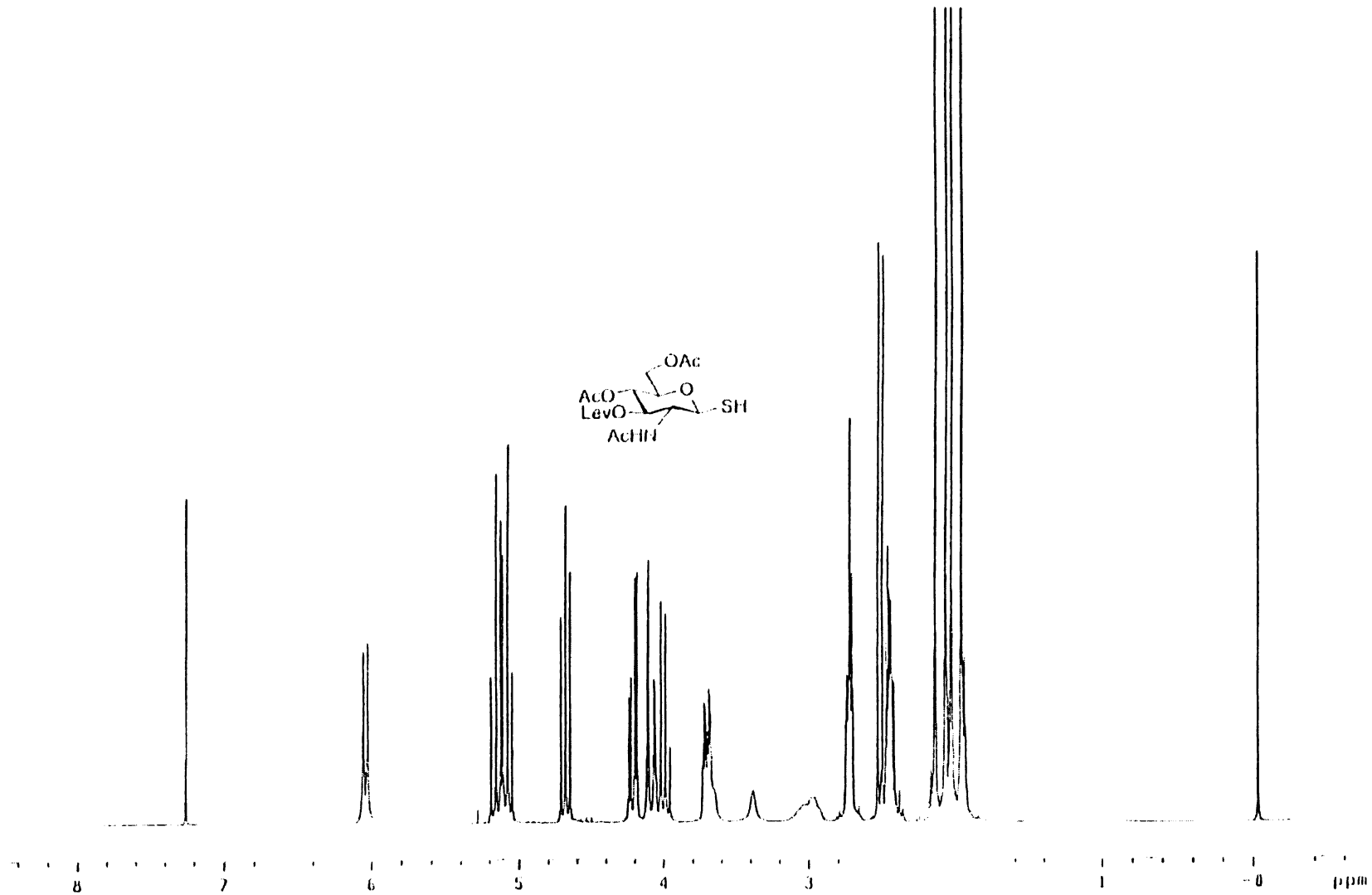
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of 2-acetamido-1,2-dideoxy-1-ethyldithio-3-*O*-levulinoyl-4,6-*O*-*p*-methoxybenzylidene-β-D-glucopyranose (**124**).



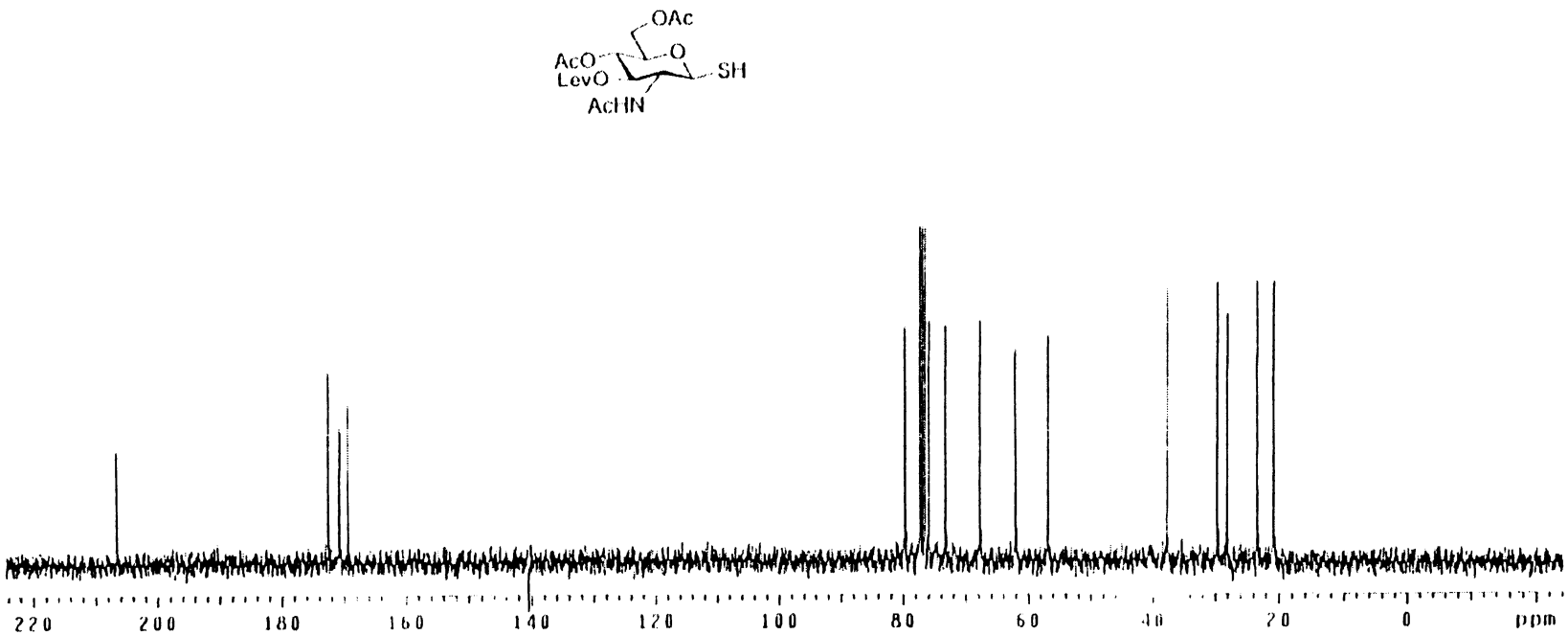
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2-acetamido-4,6-di-*O*-acetyl-1,2-dideoxy-1-ethyldithio-3-*O*-levulinoyl-β-D-glucopyranose (**126**).



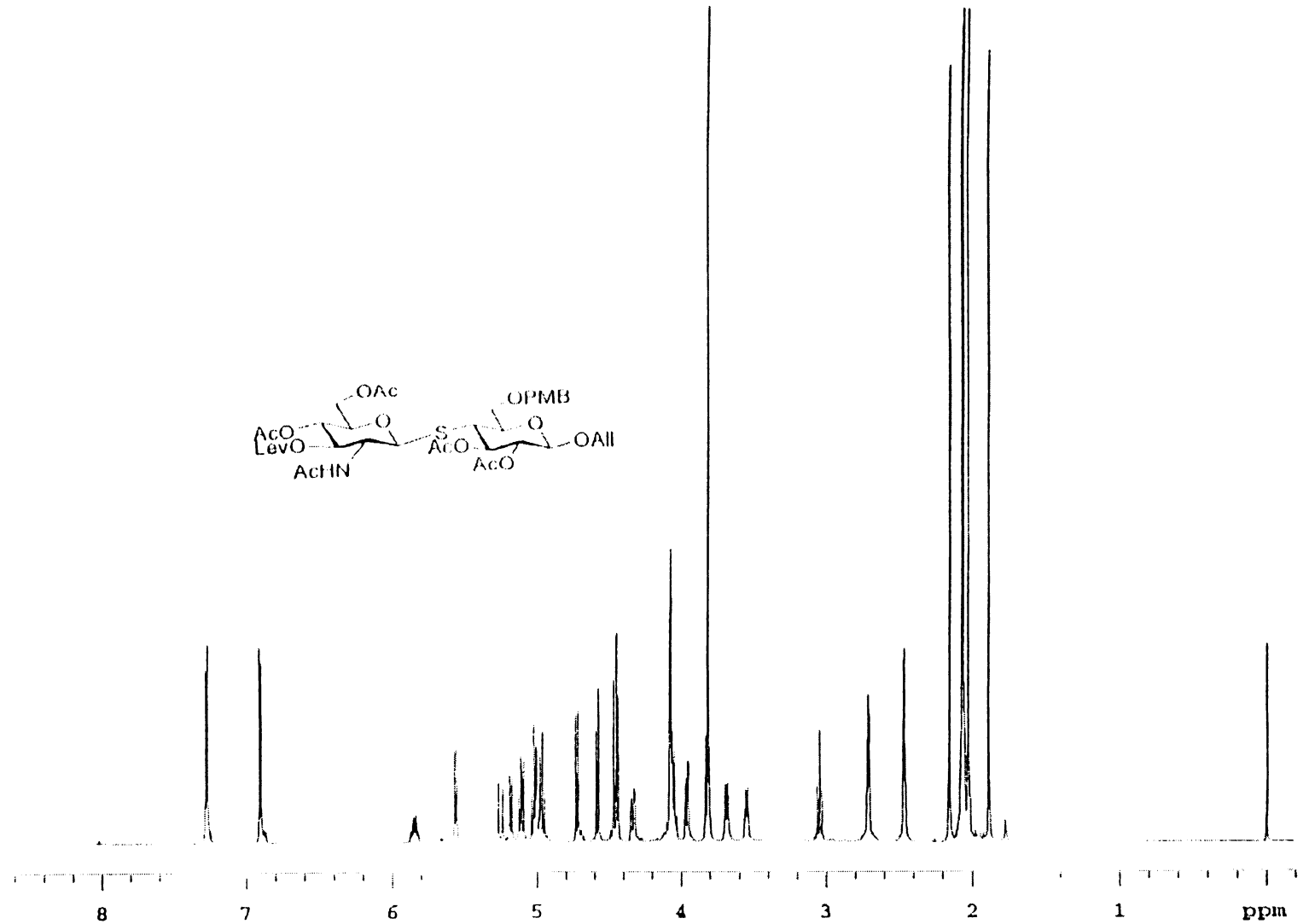
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of 2-acetamido-4,6-di-*O*-acetyl-1,2-dideoxy-1-ethyldithio-3-*O*-levulinoyl-β-D-glucopyranose (**126**).



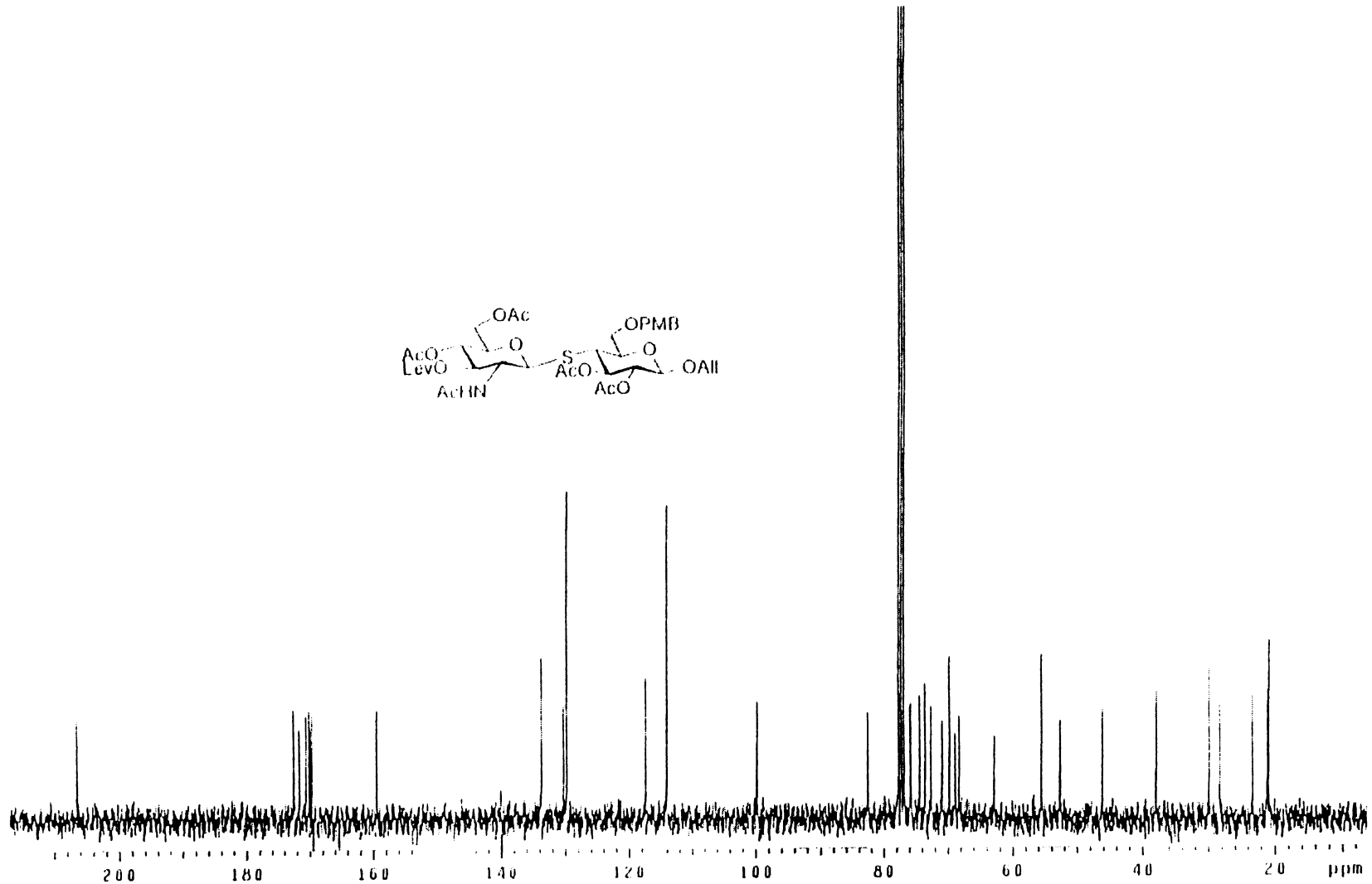
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-1-thio-β-D-glucopyranose (**65**).



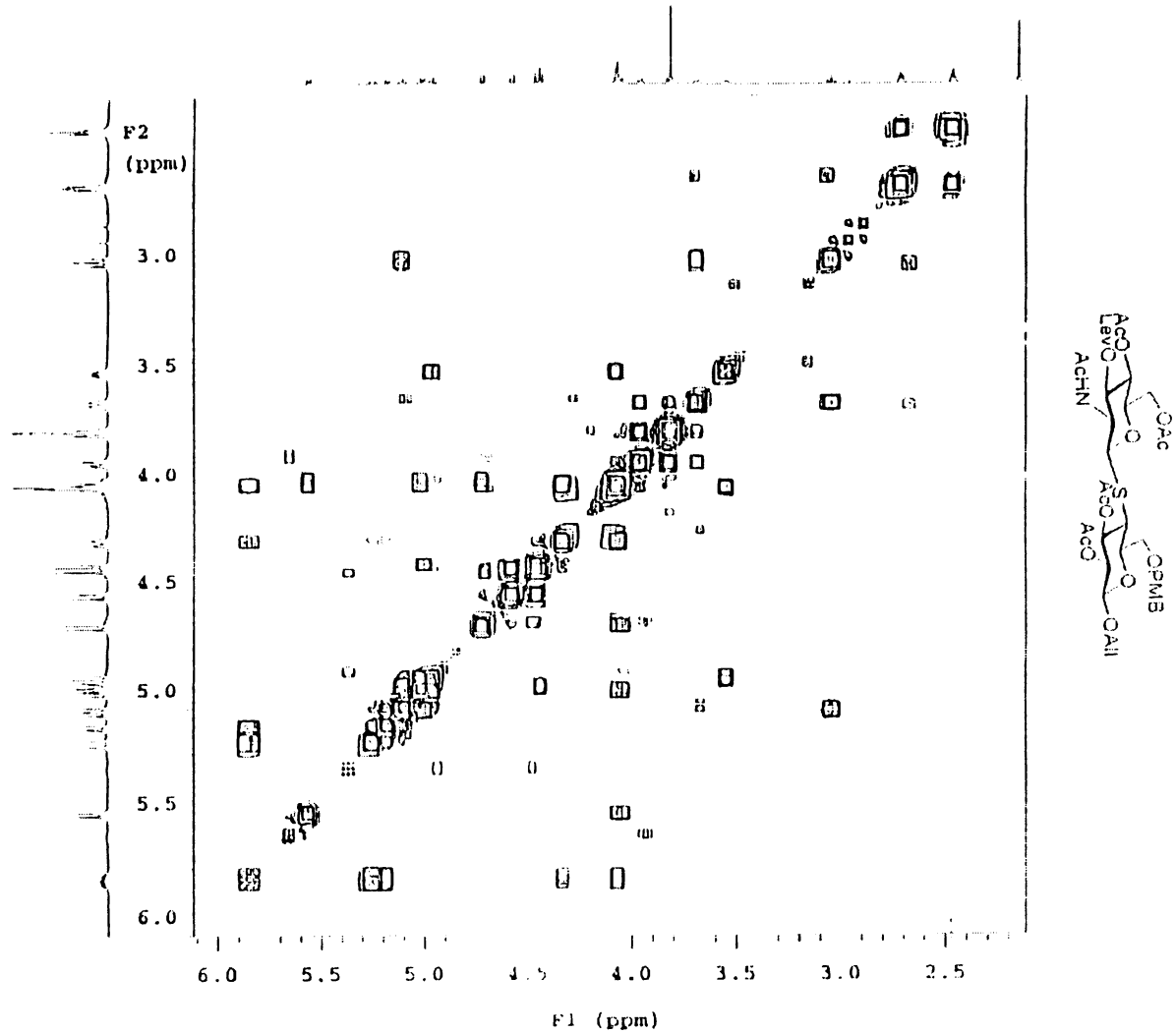
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of 2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-1-thio-β-D-glucopyranose (**65**).



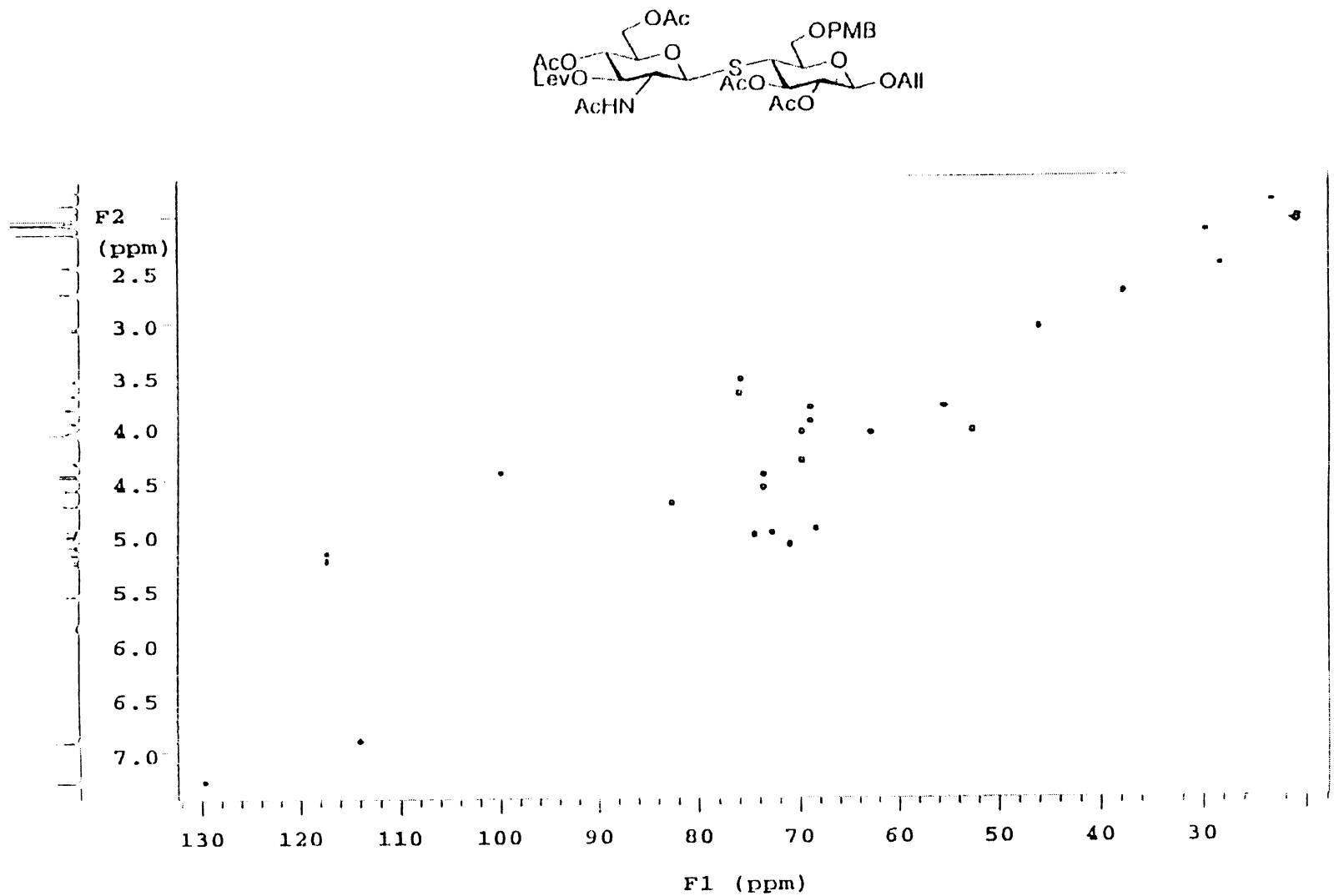
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**64**).



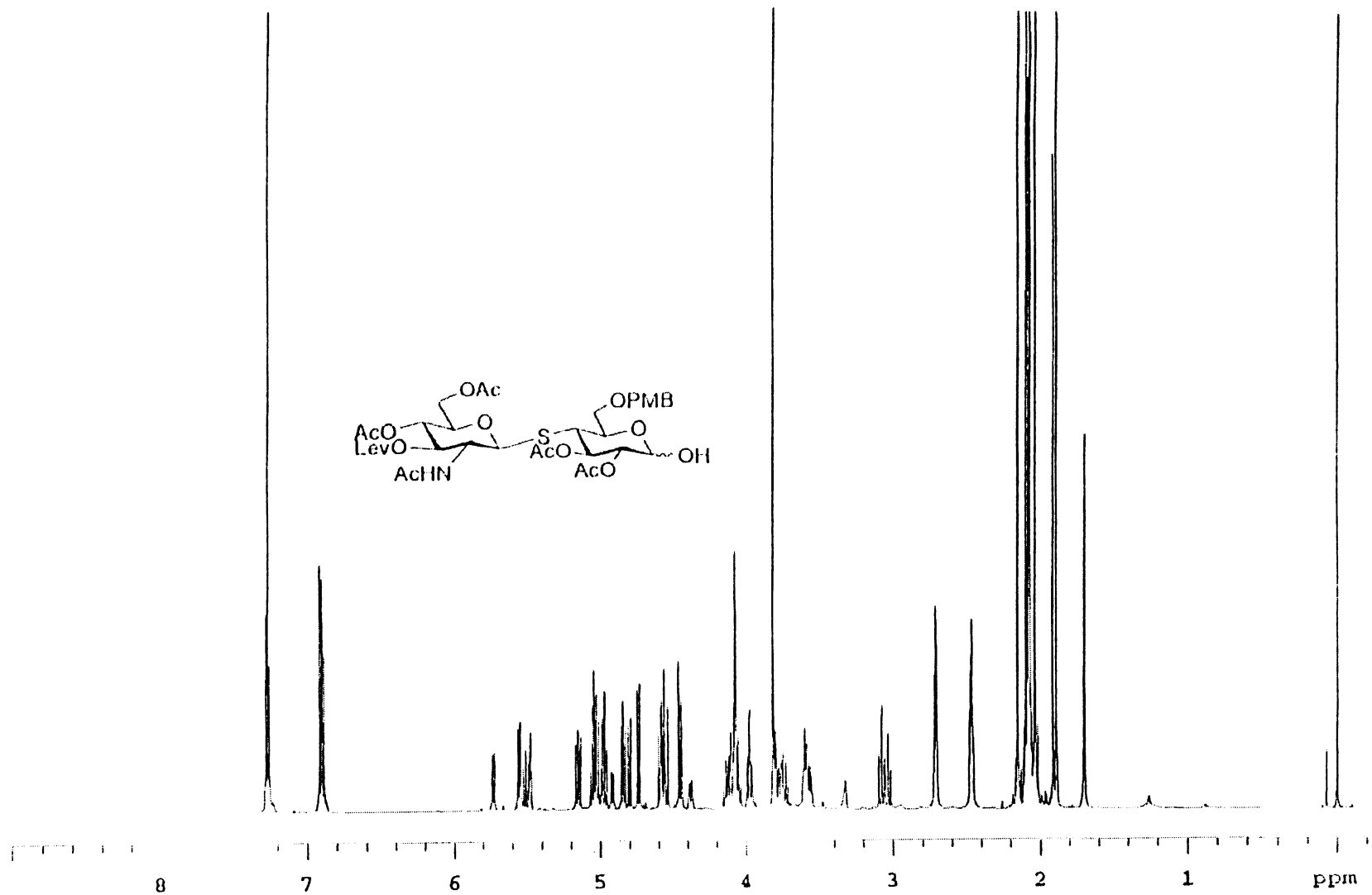
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**64**).



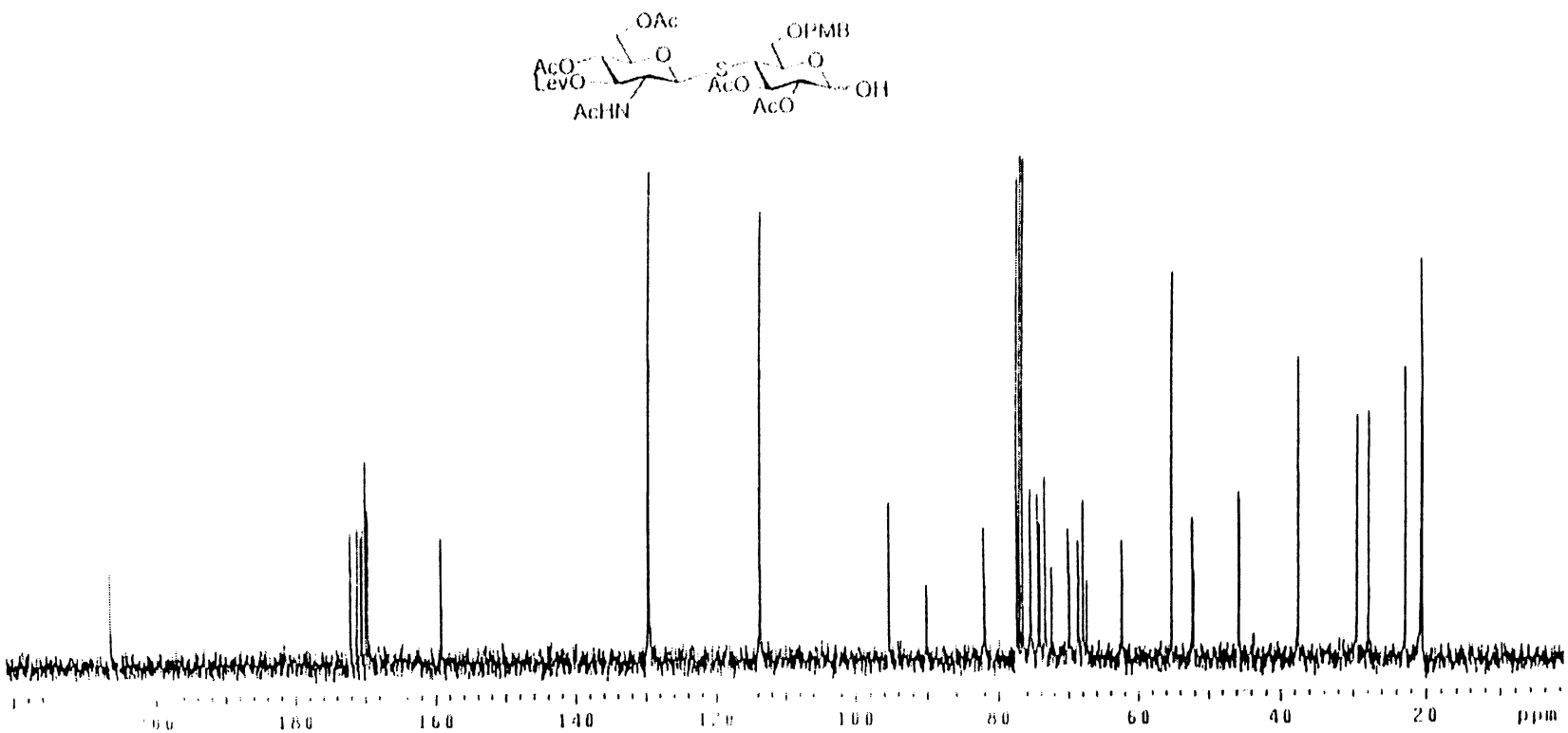
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**64**).



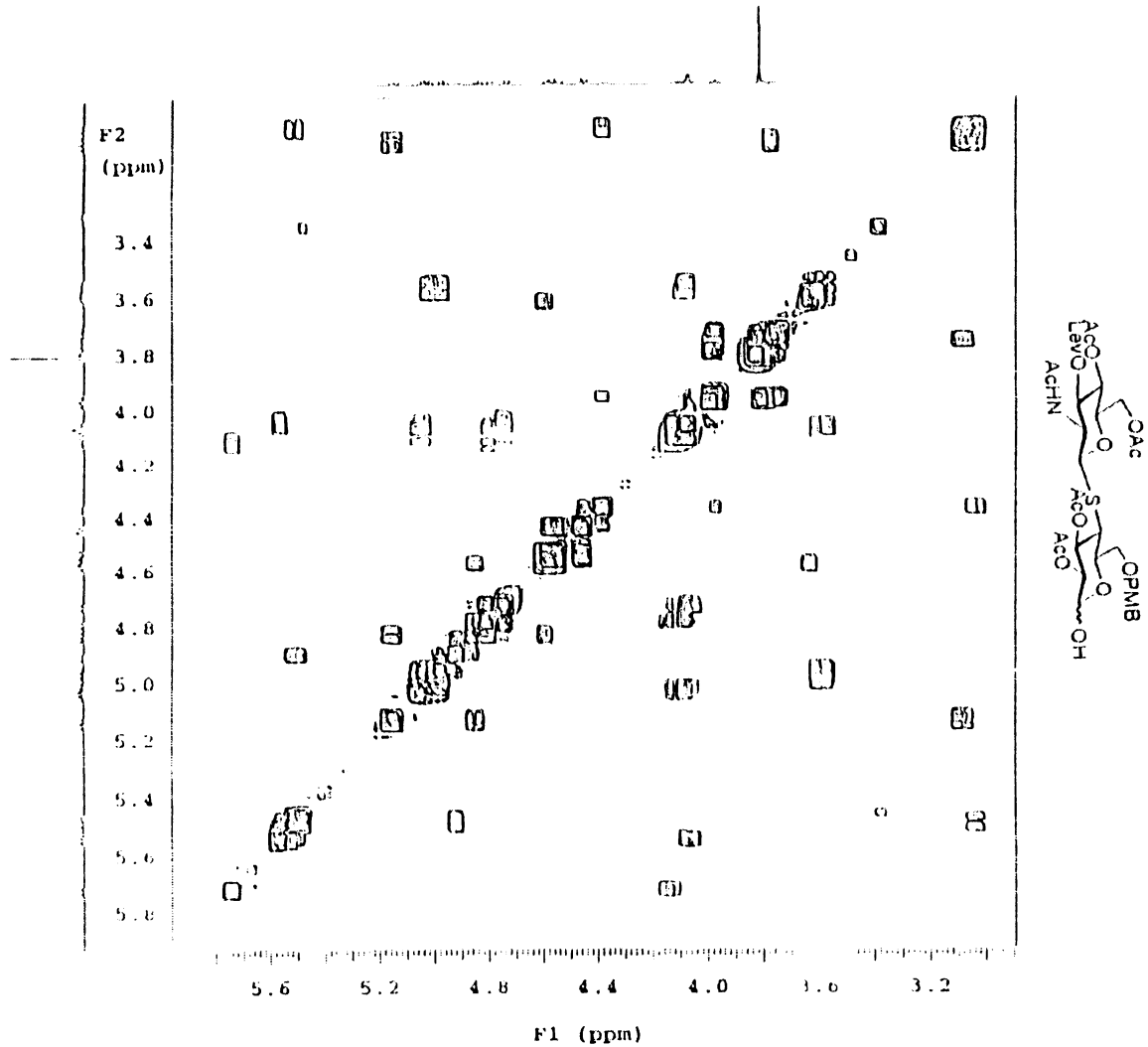
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**64**).



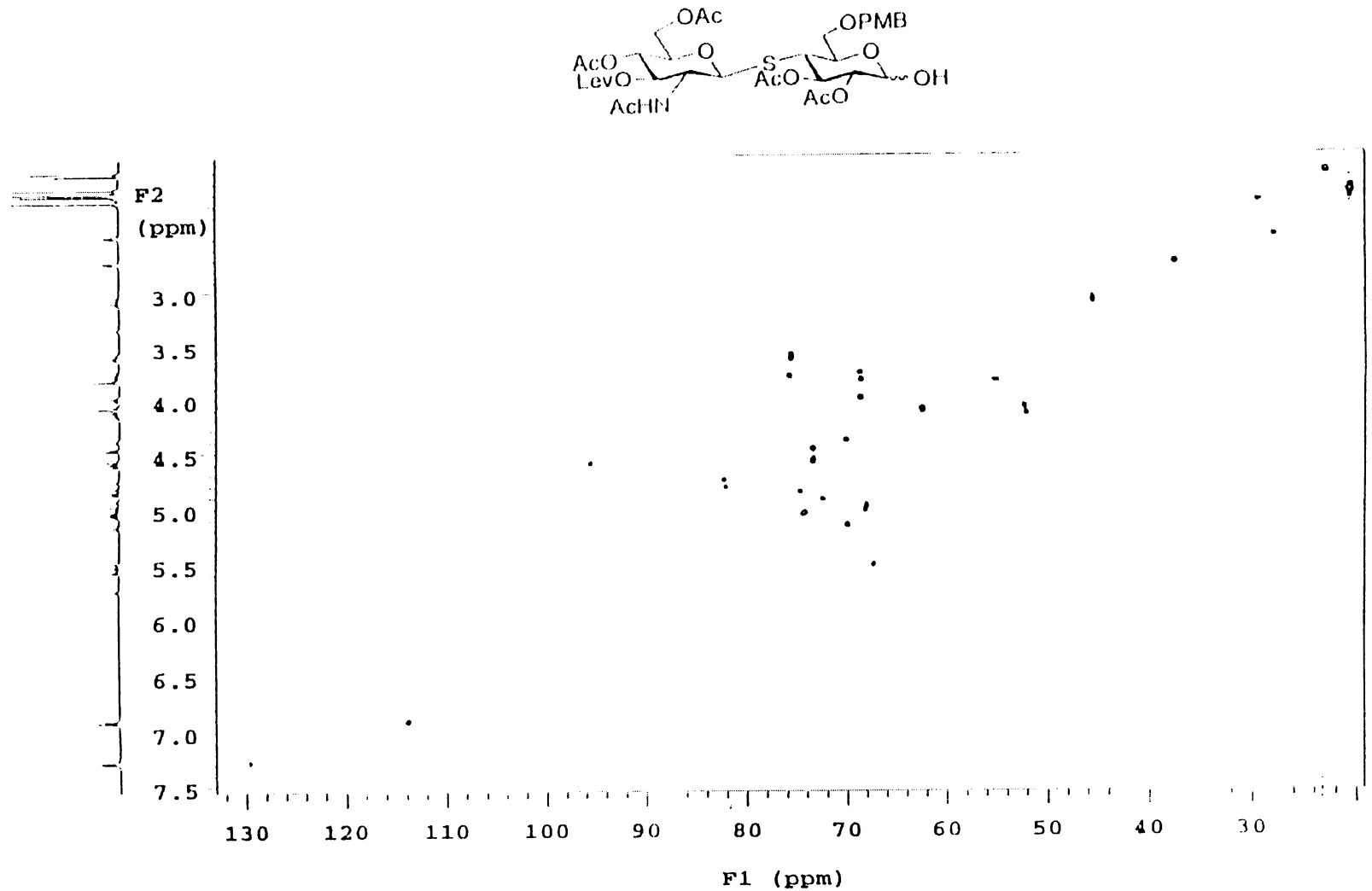
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α,β-D-glucopyranoside (**127**).



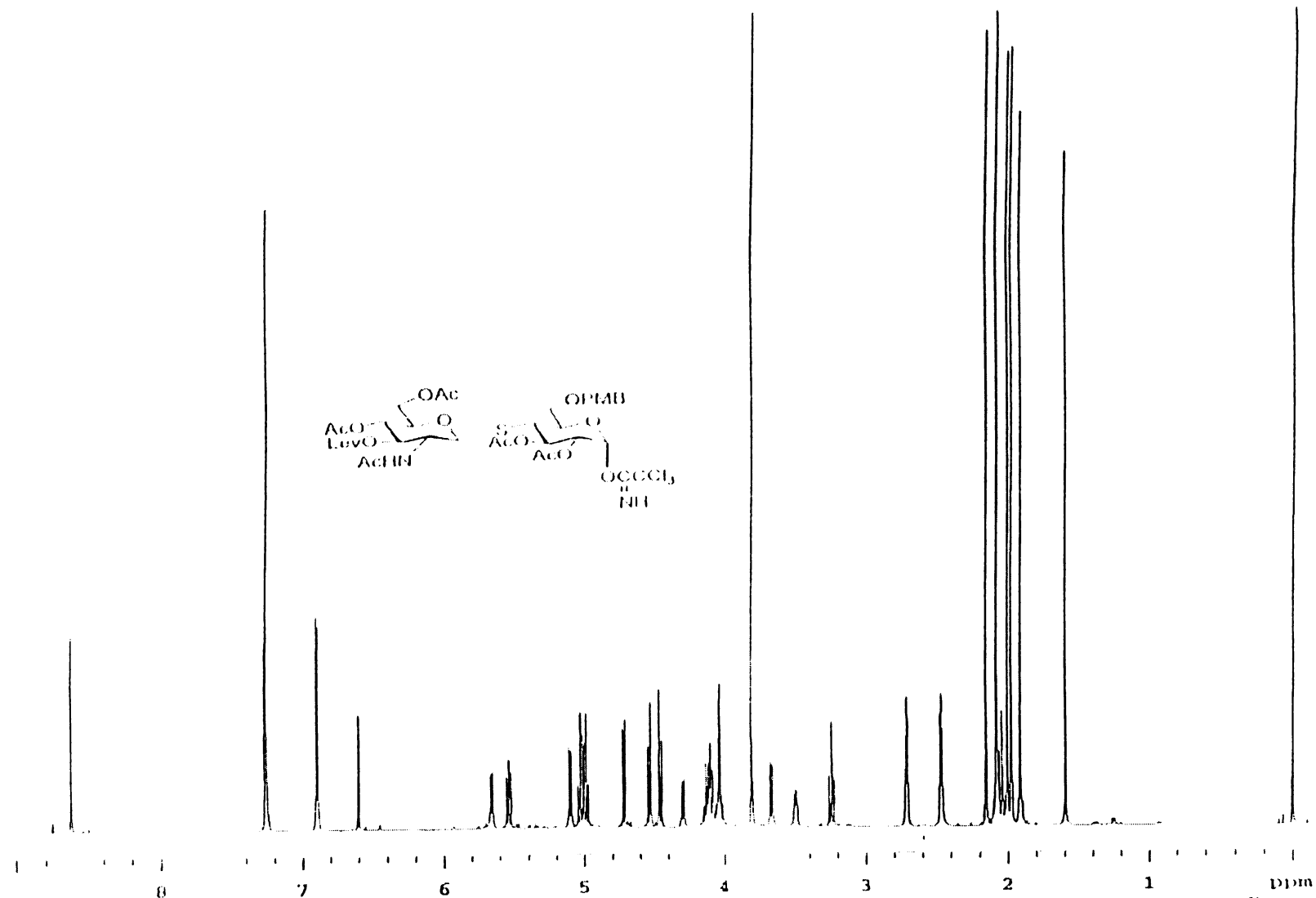
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α β-D-glucopyranoside (**127**).



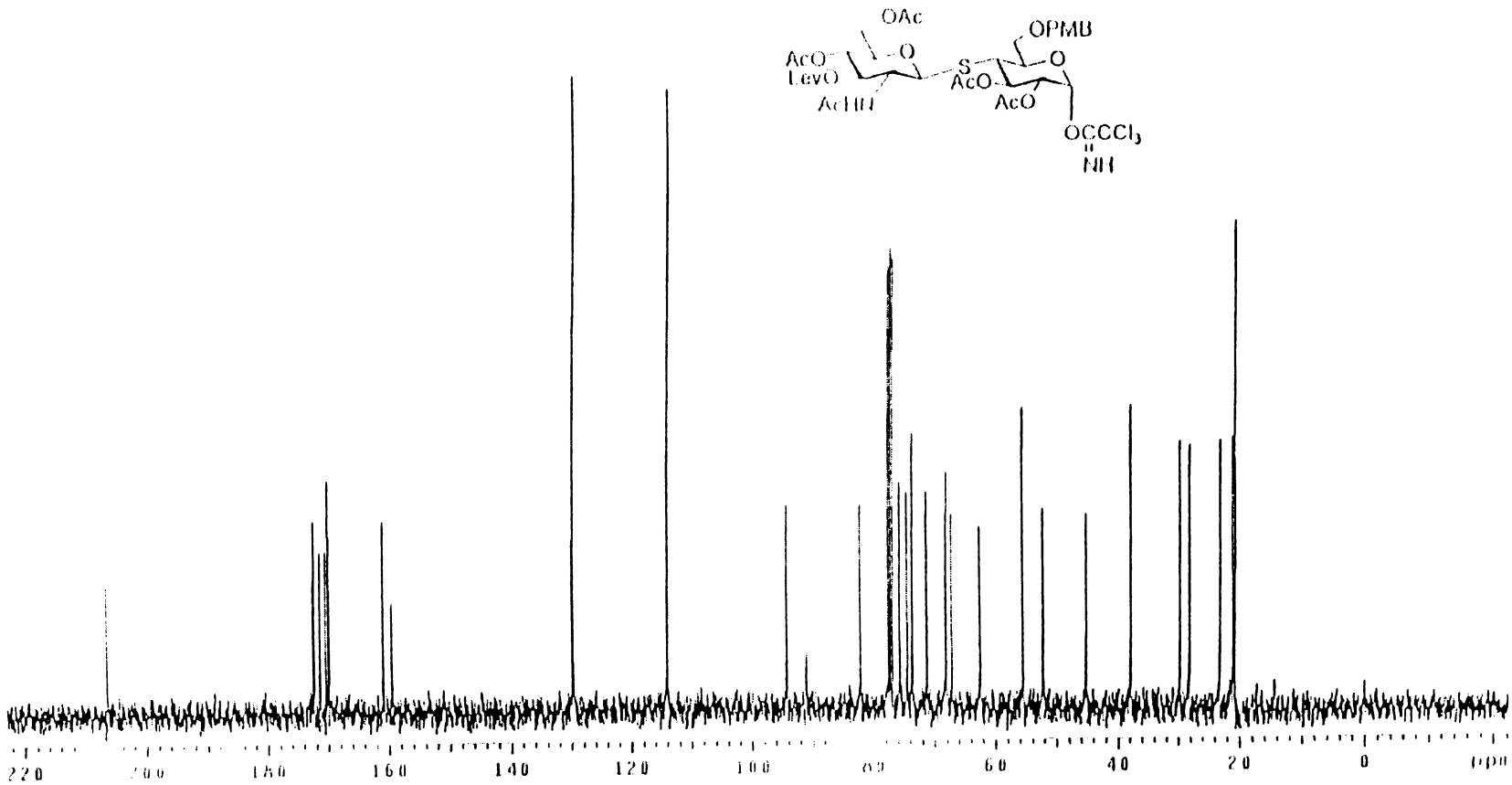
gCOSY spectrum (600 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α β-D-glucopyranoside (**127**).



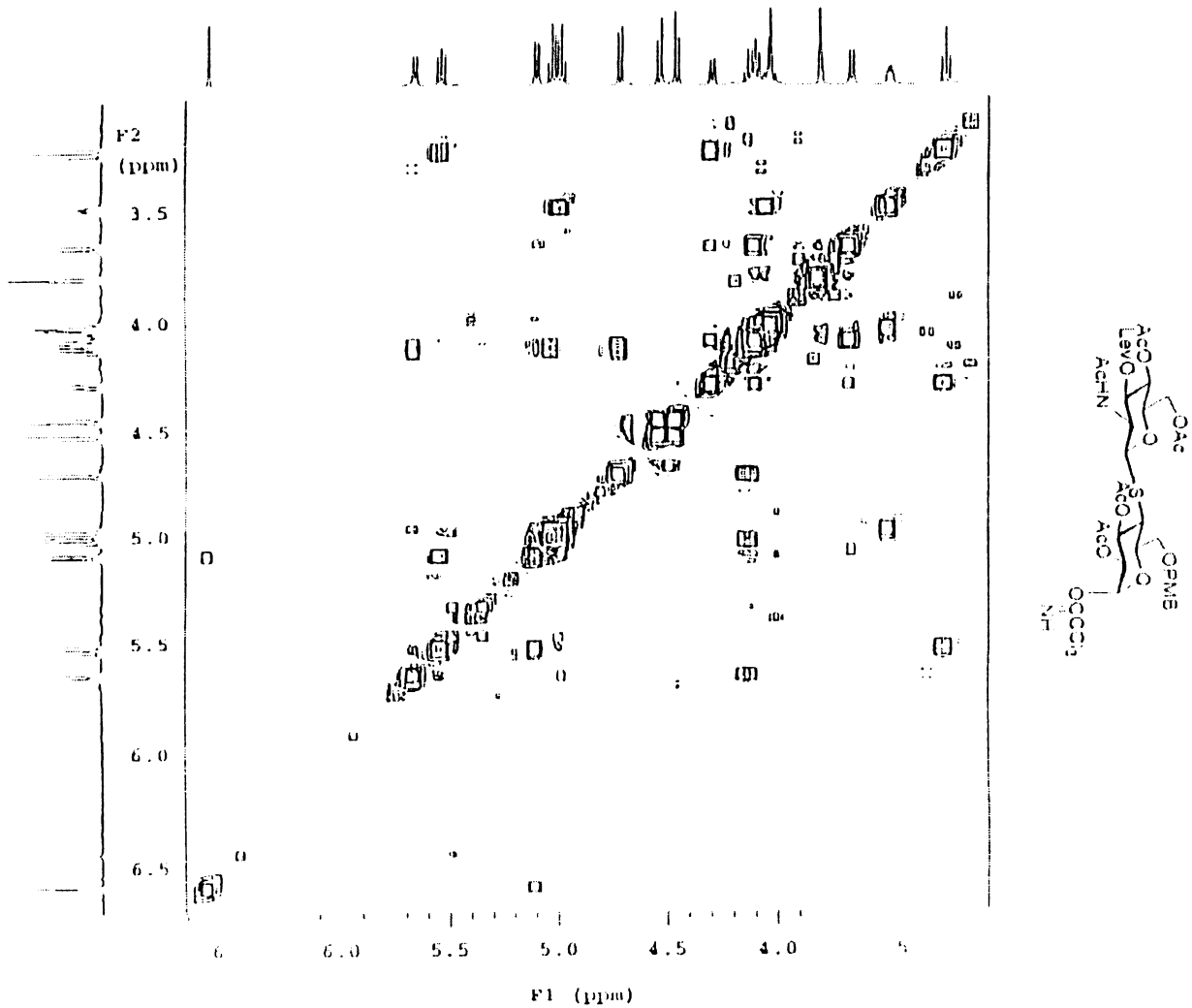
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α,β-D-glucopyranoside (**127**).



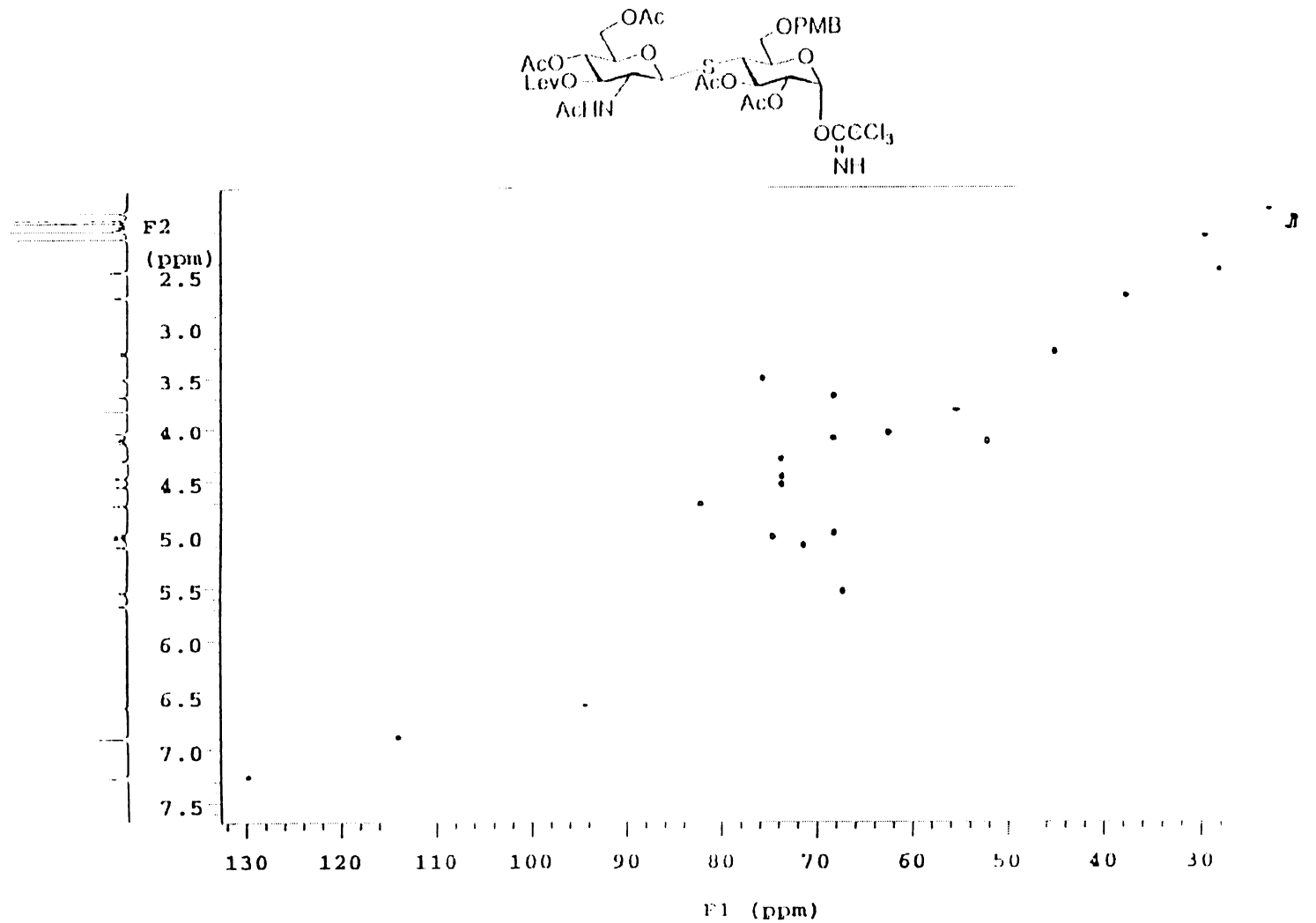
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**66**).



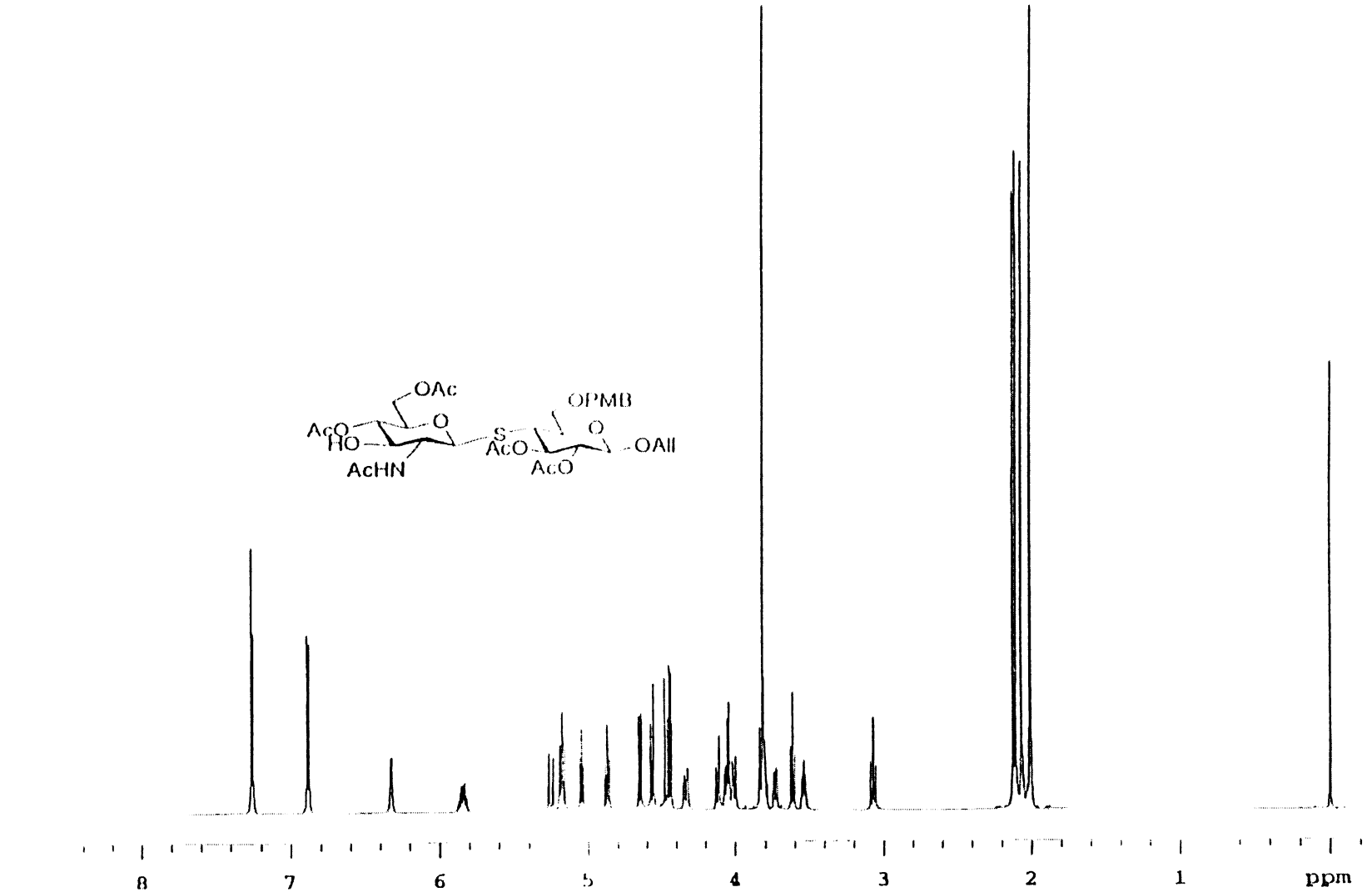
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**66**).



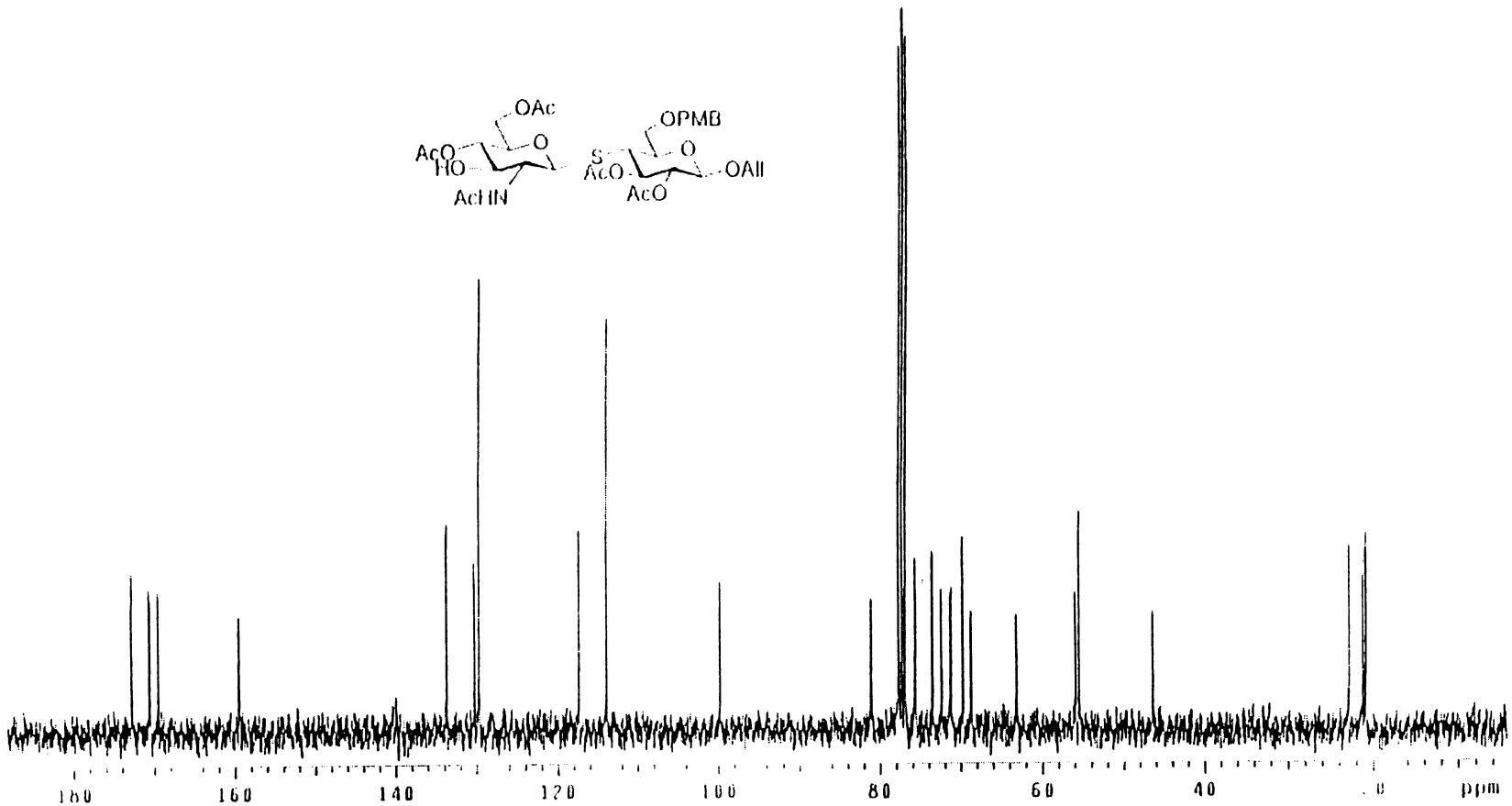
gCOSY spectrum (600 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-α-D-glucopyranosyl trichloroacetimidate (**66**).



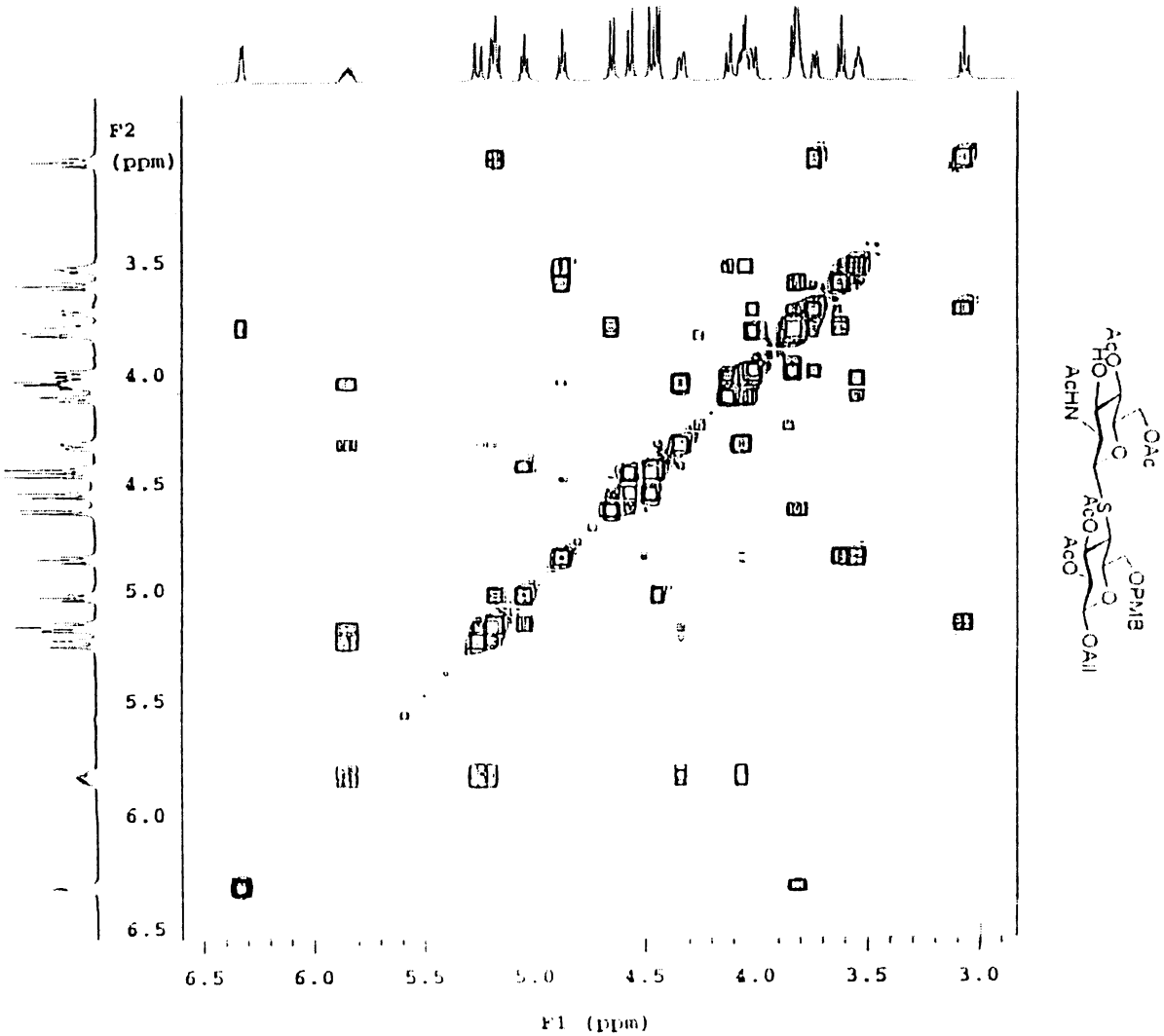
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*α*-D-glucopyranosyl trichloroacetimidate (**66**).



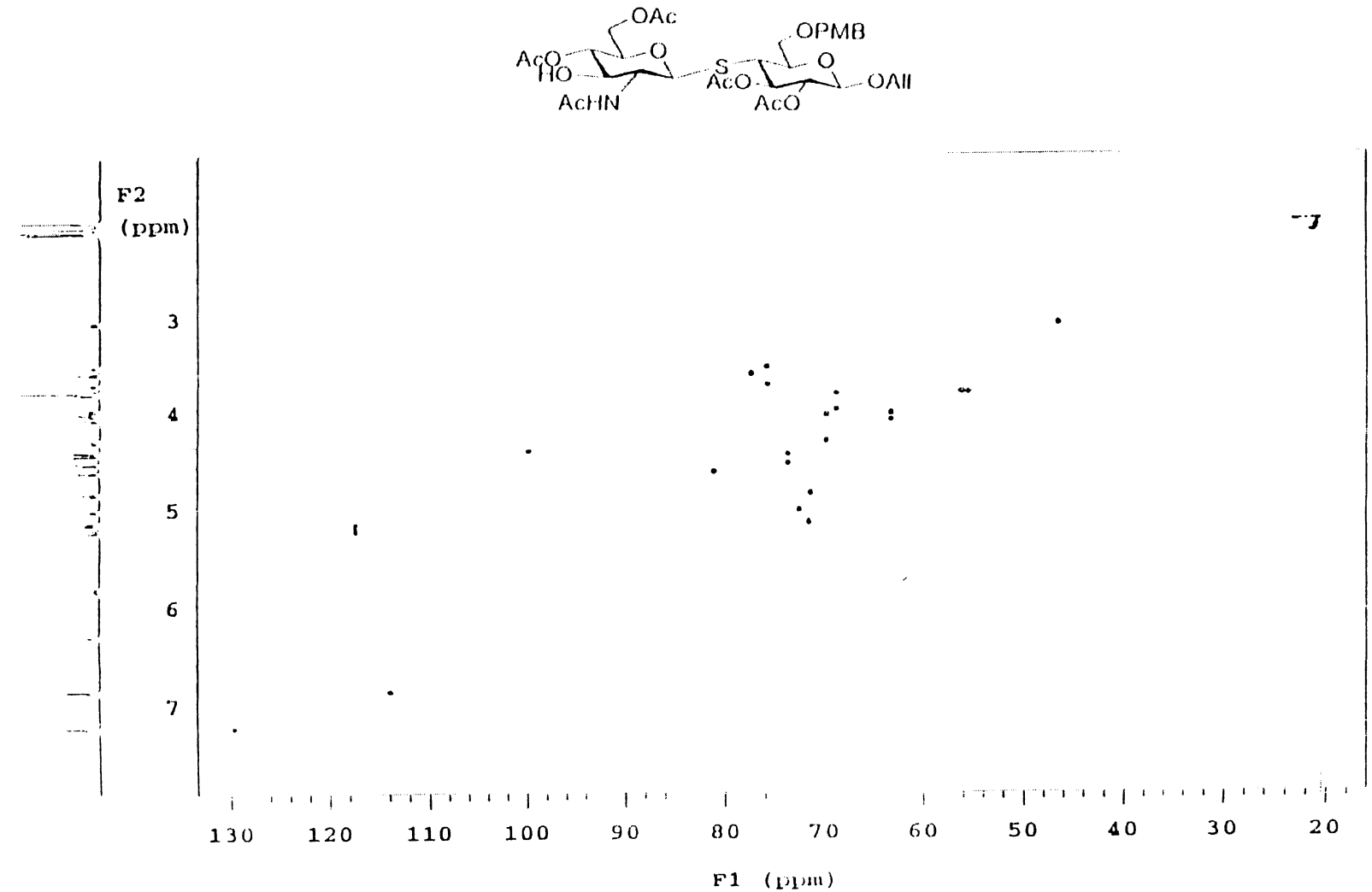
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**67**).



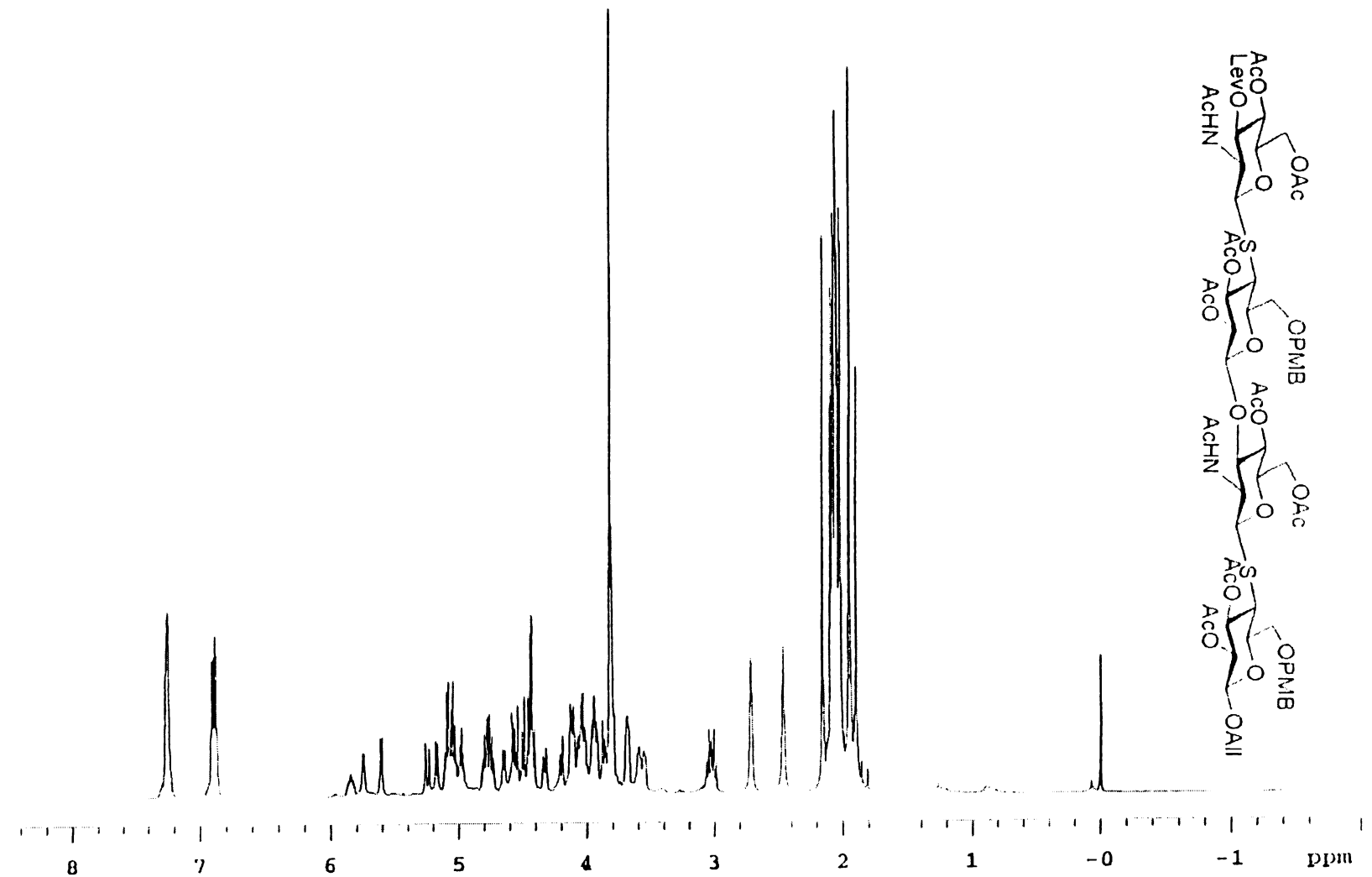
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**67**).



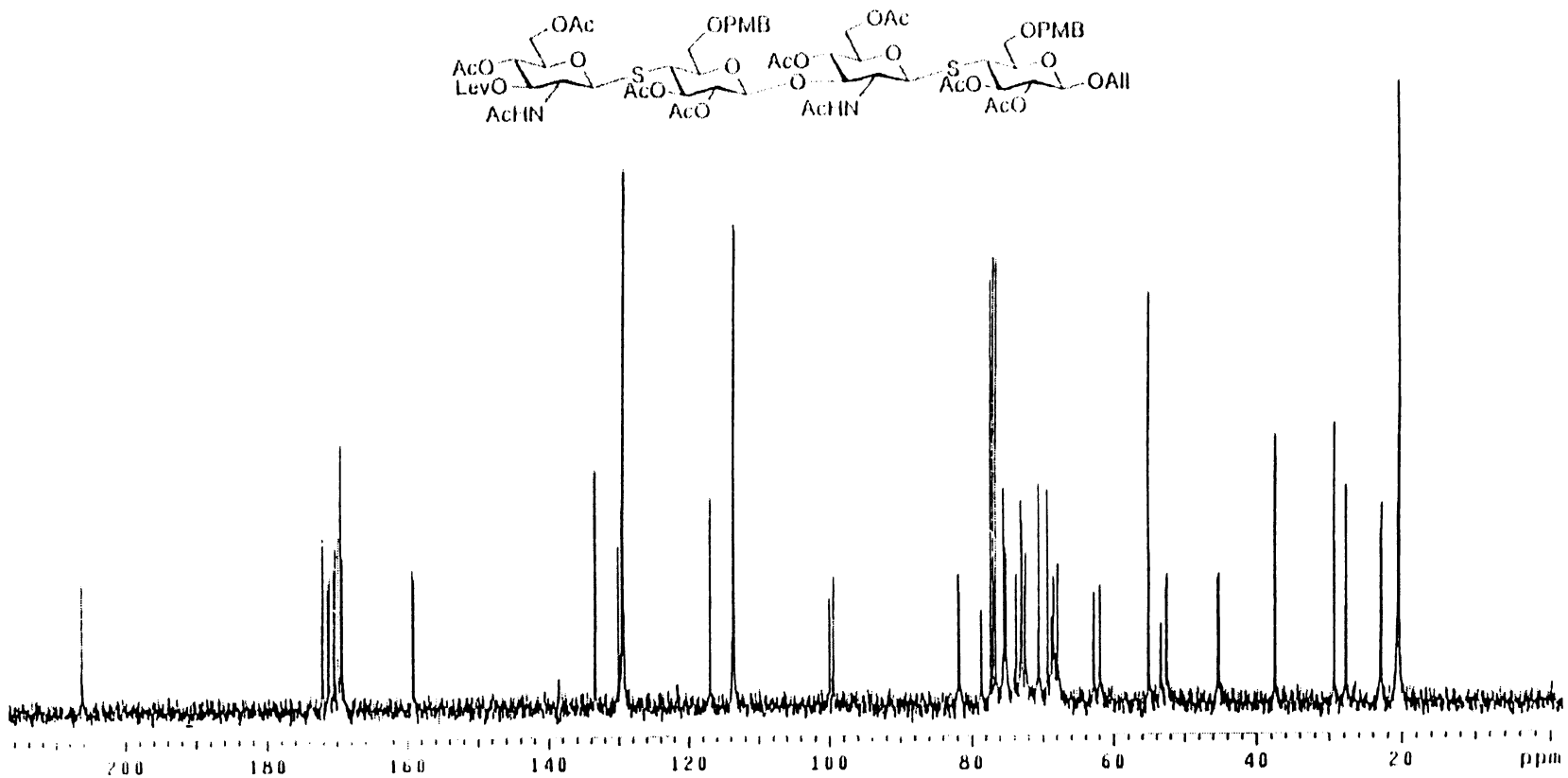
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**67**).



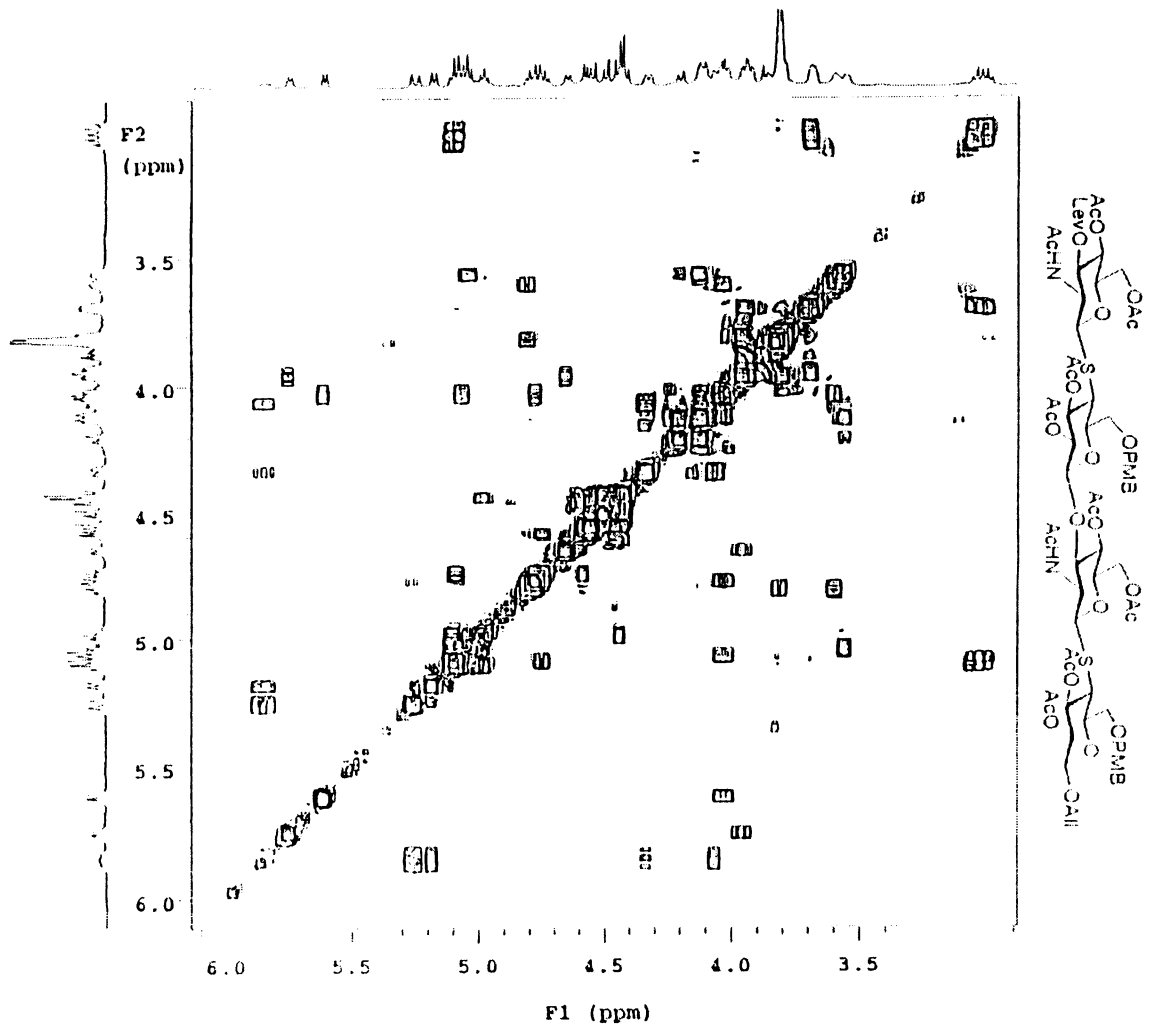
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-β-D-glucopyranoside (**67**).



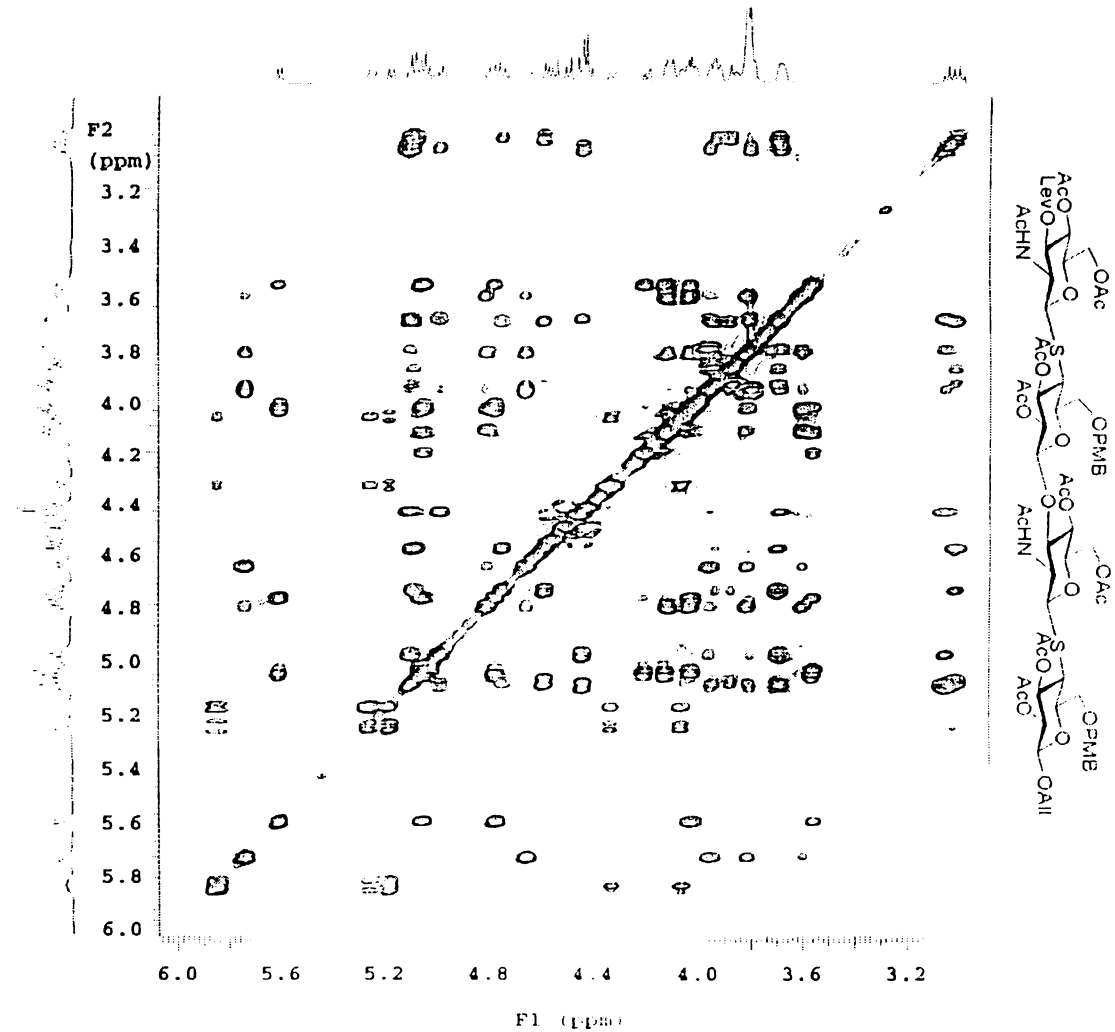
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**128**).



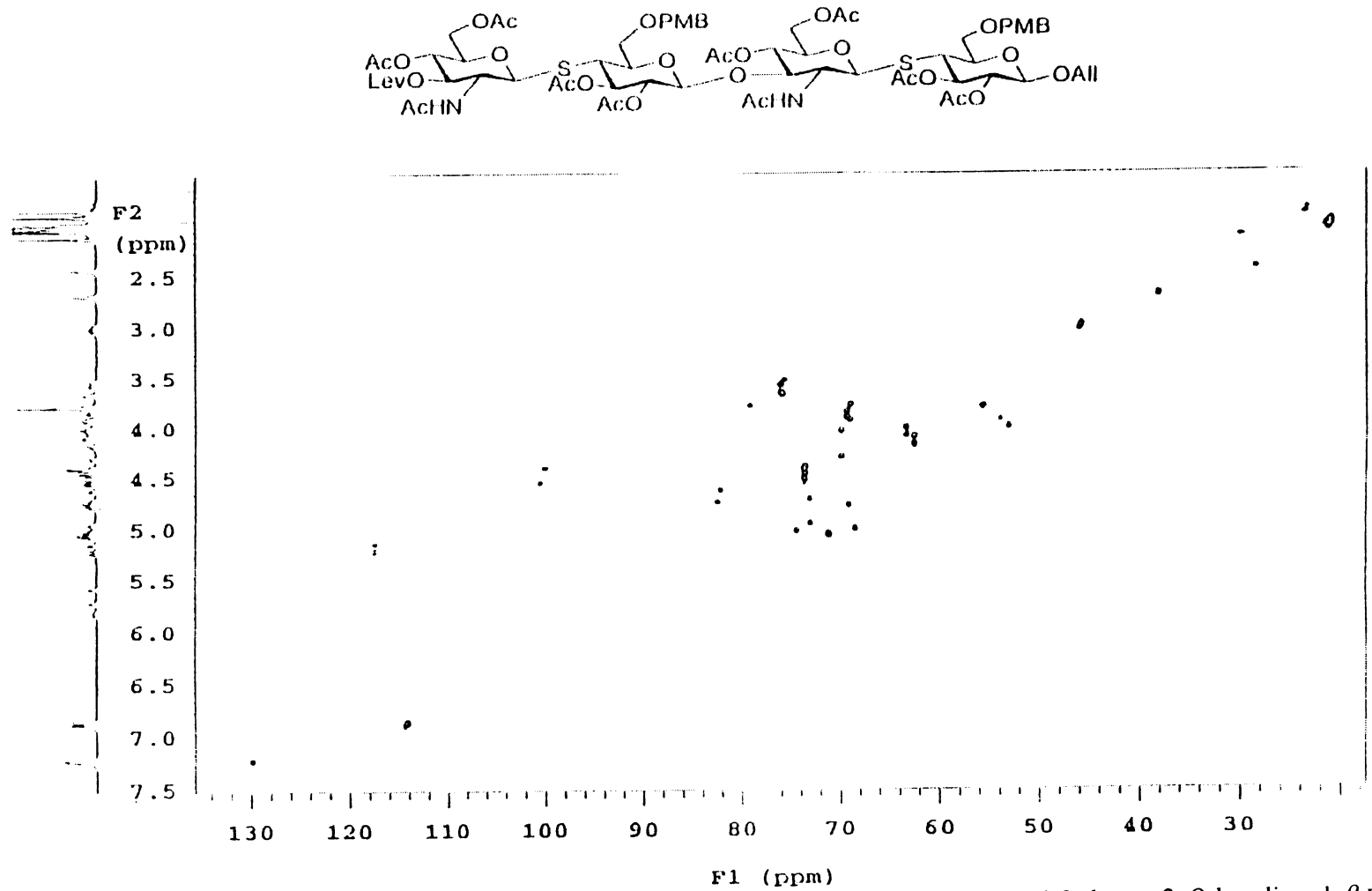
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**128**).



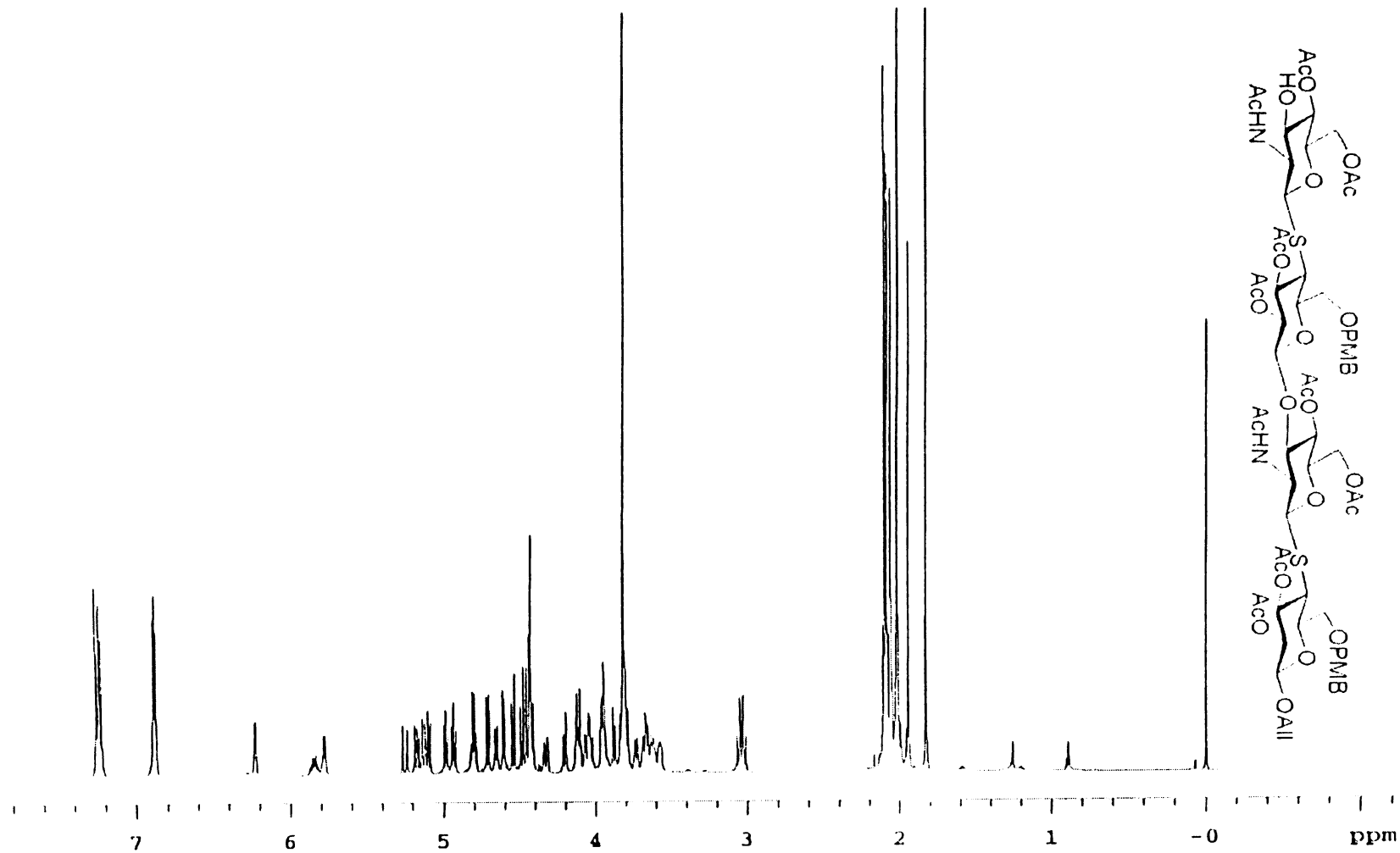
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**128**).



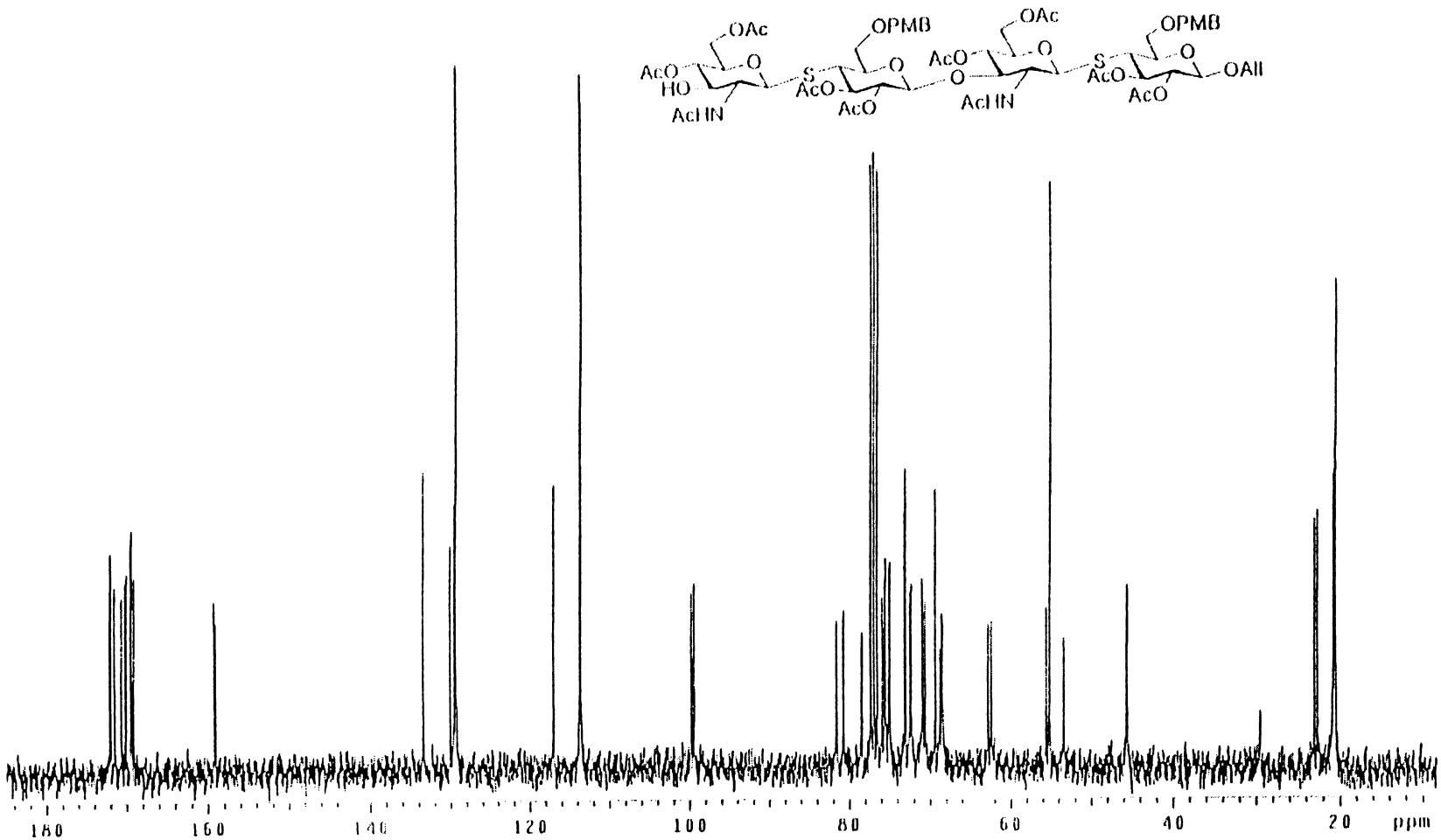
TOCSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**128**).



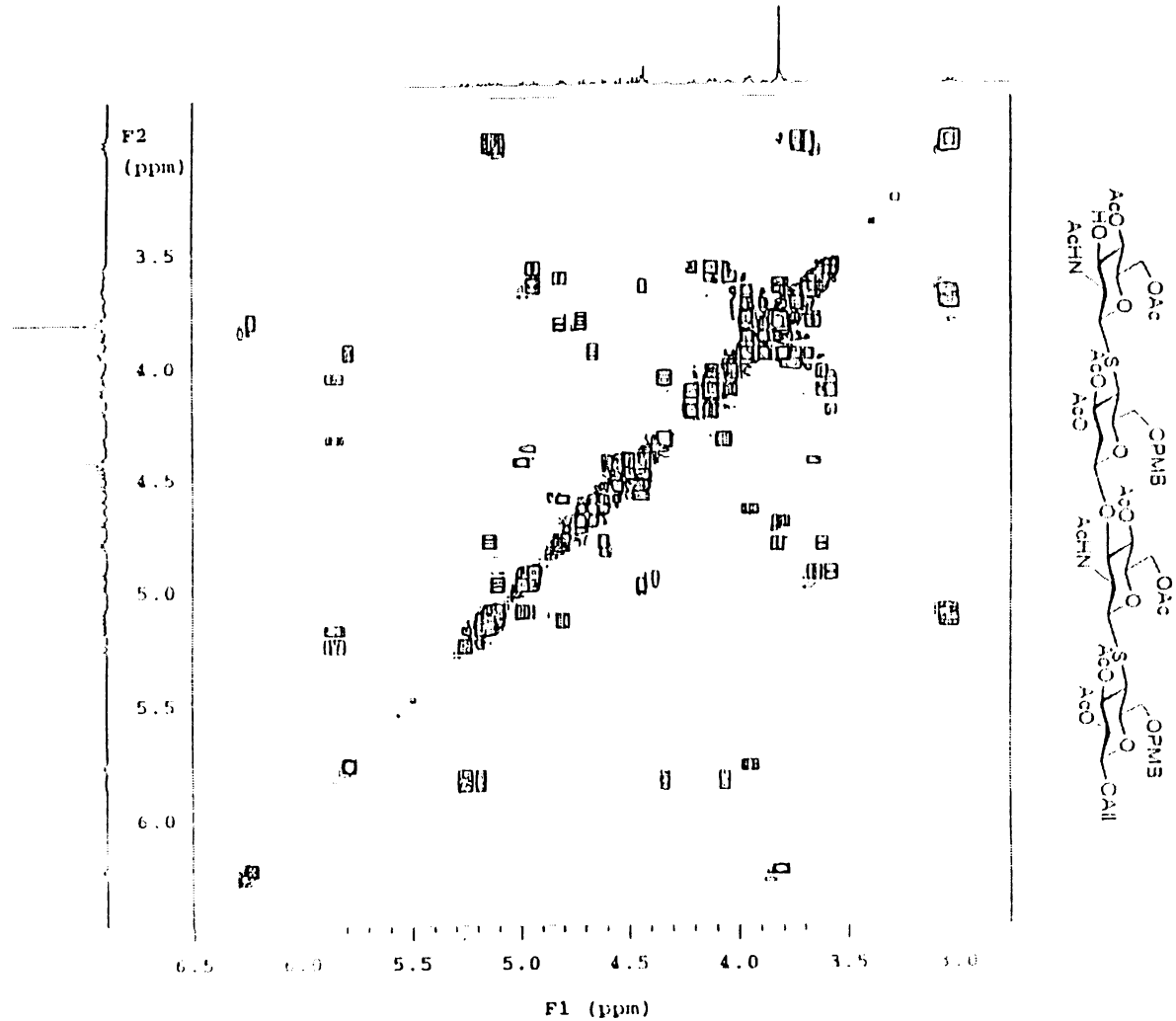
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**128**).



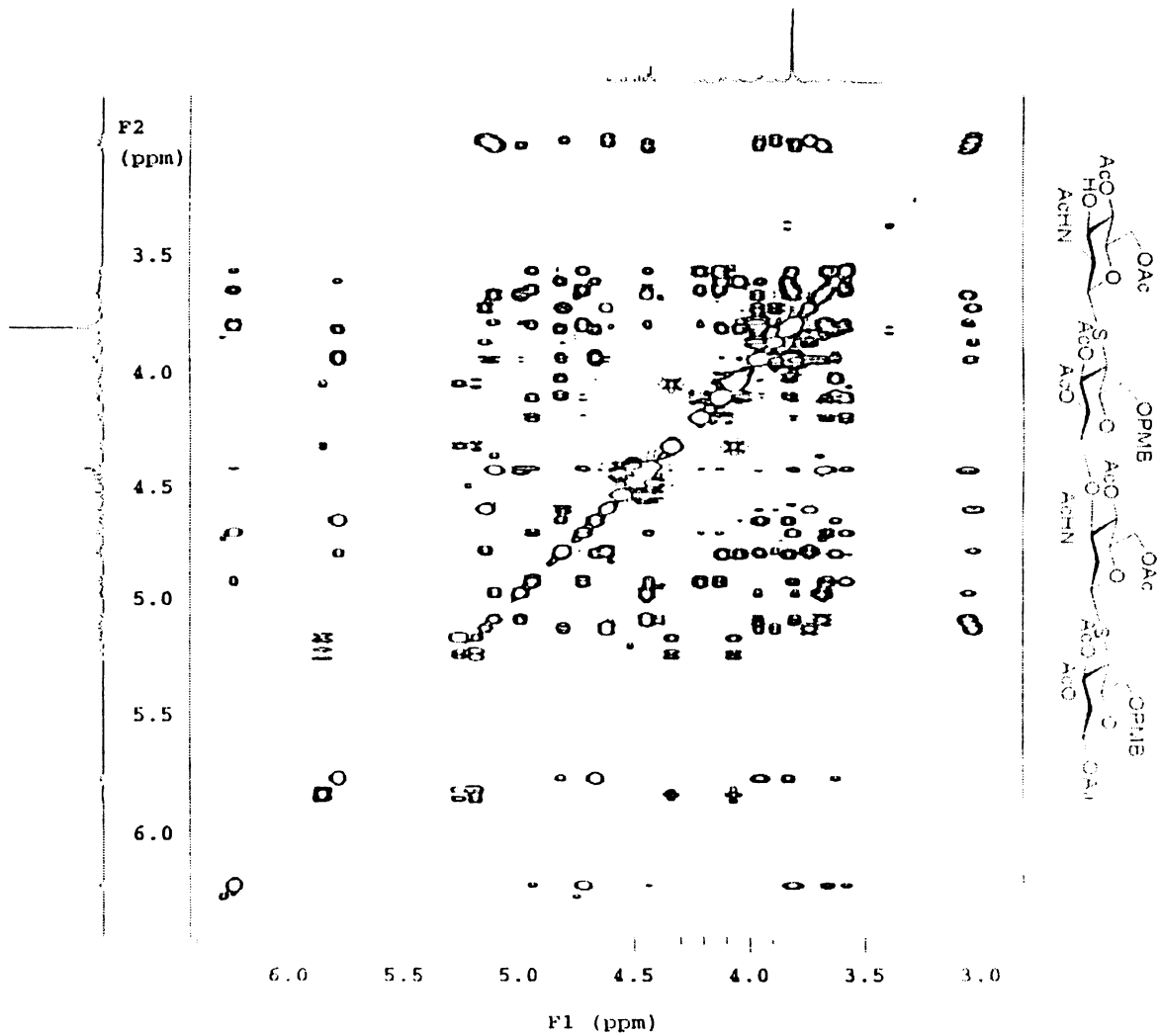
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**129**).



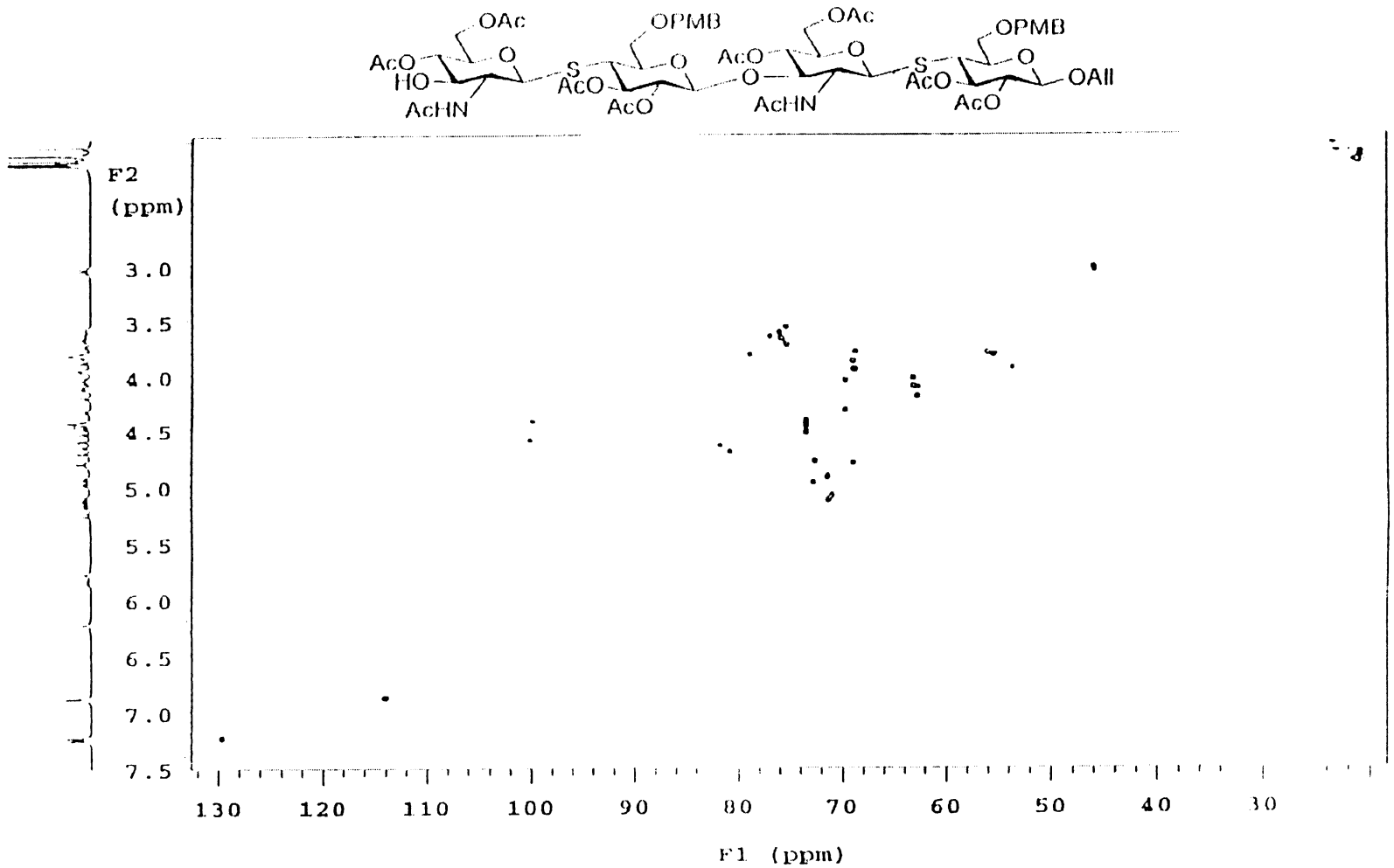
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**129**).



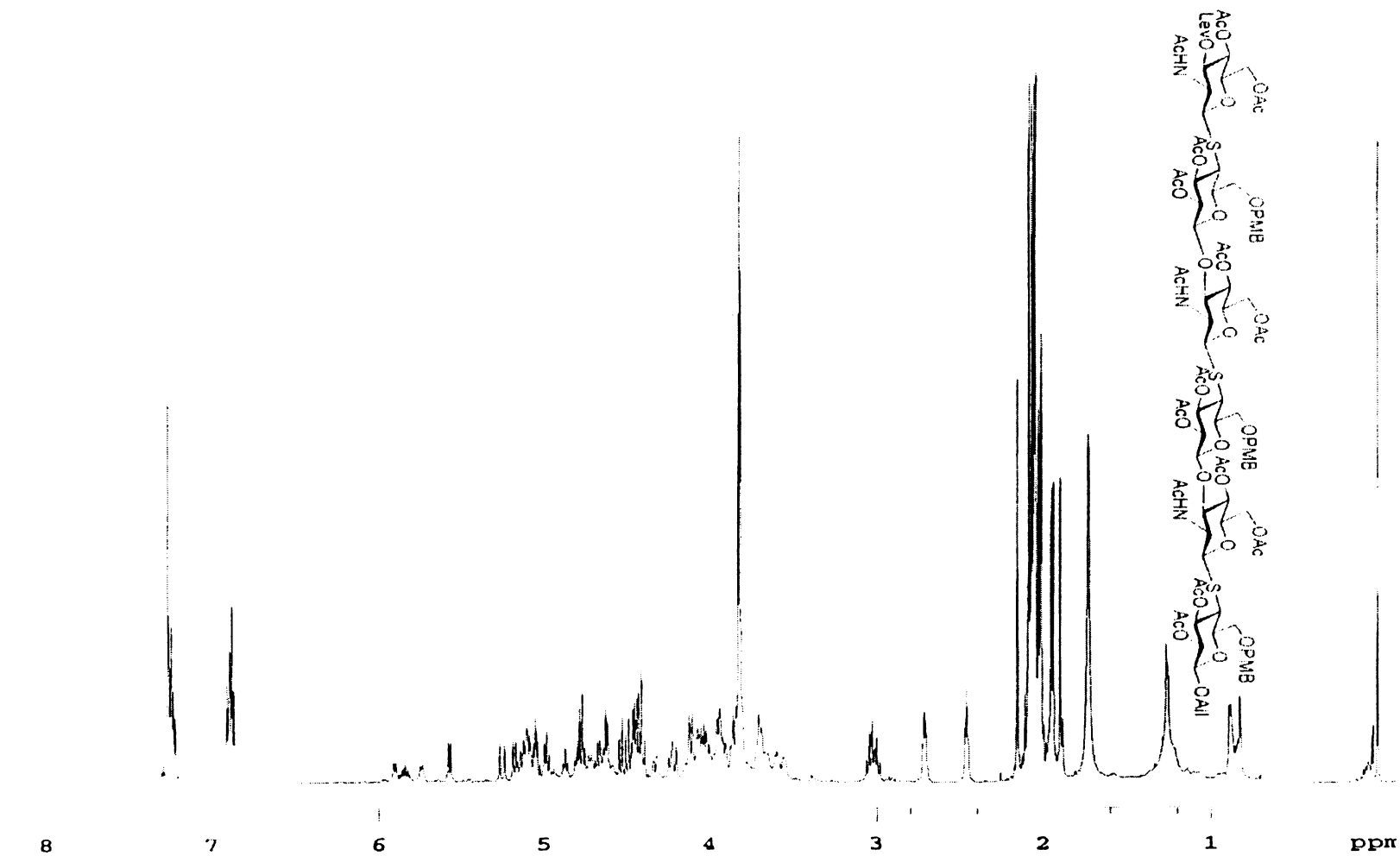
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**129**).



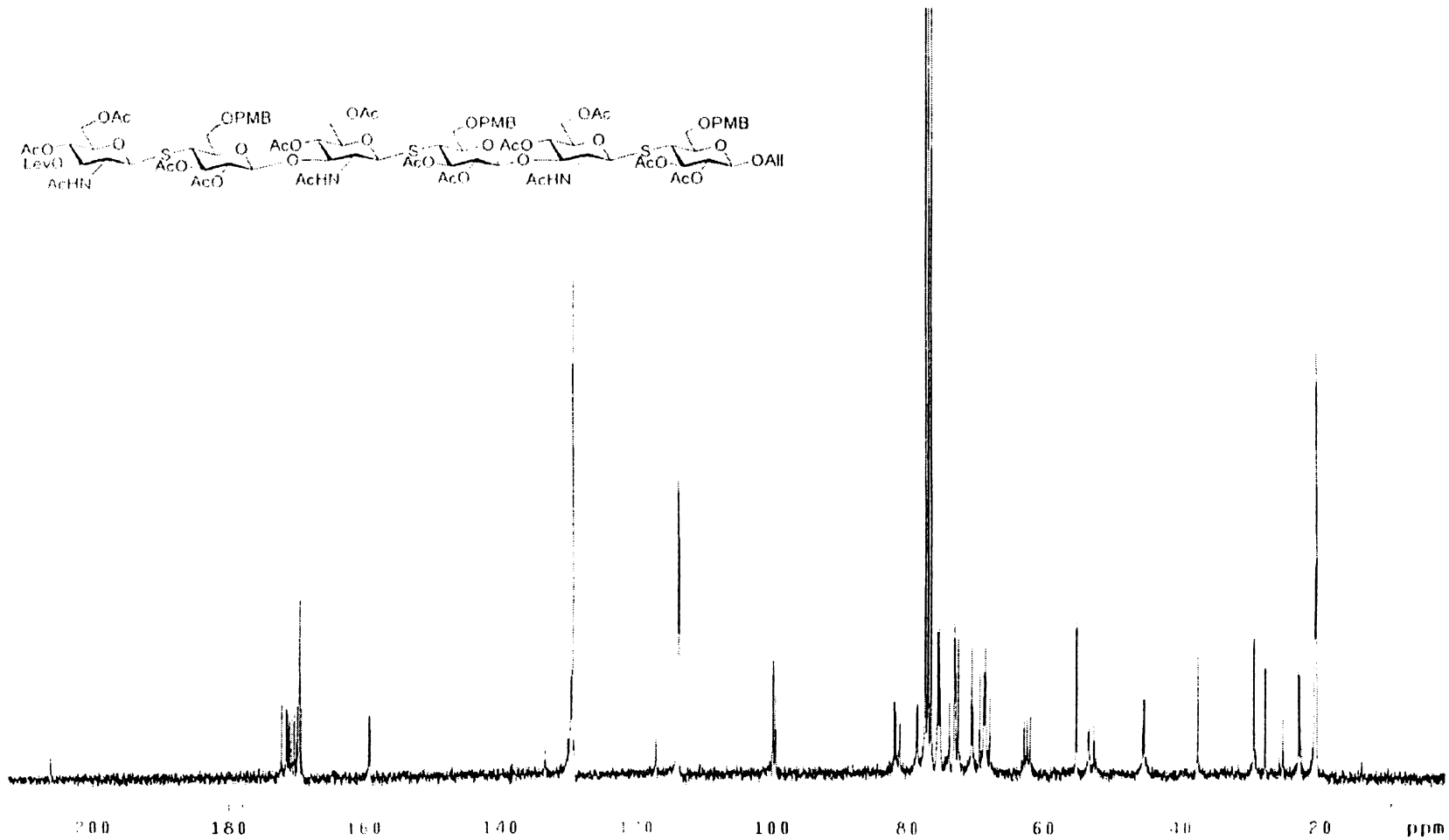
TOCSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**129**).



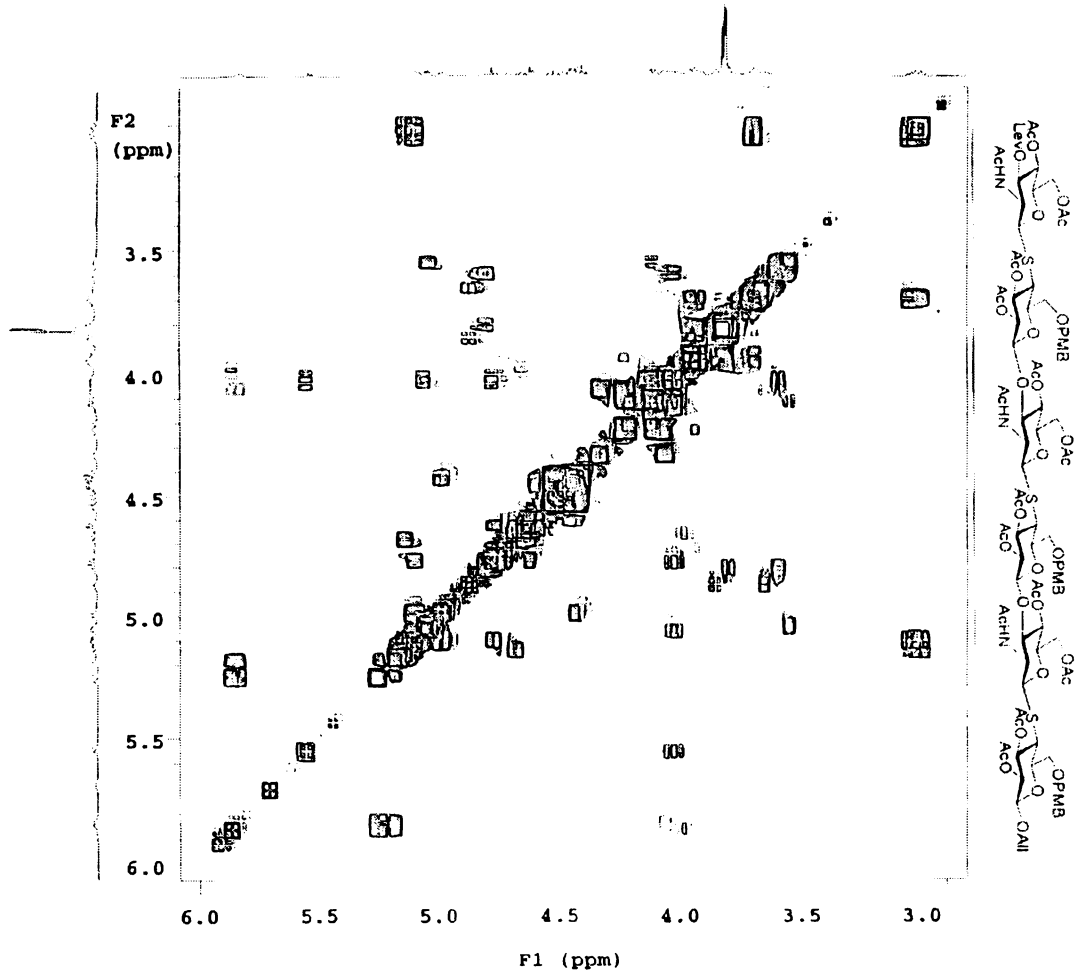
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**129**).



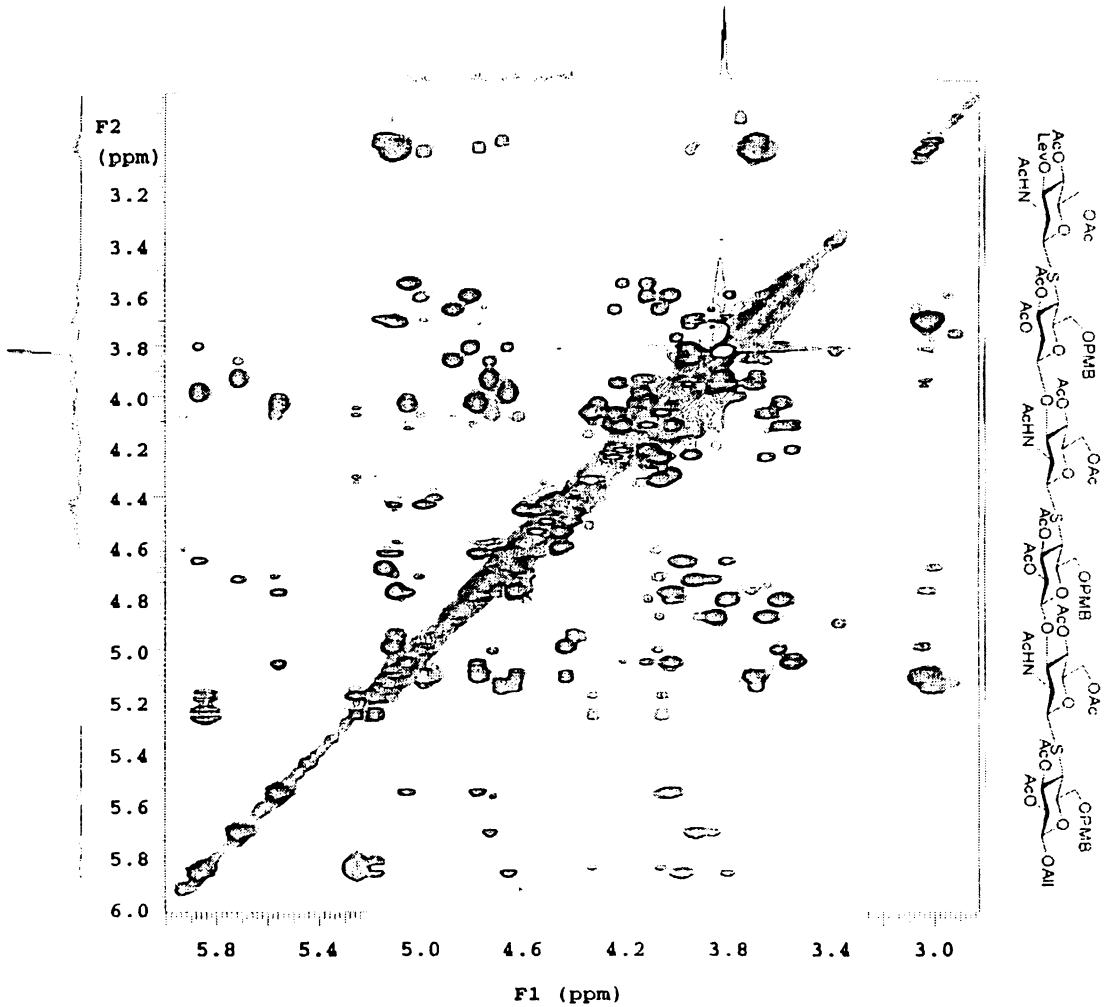
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**130**).



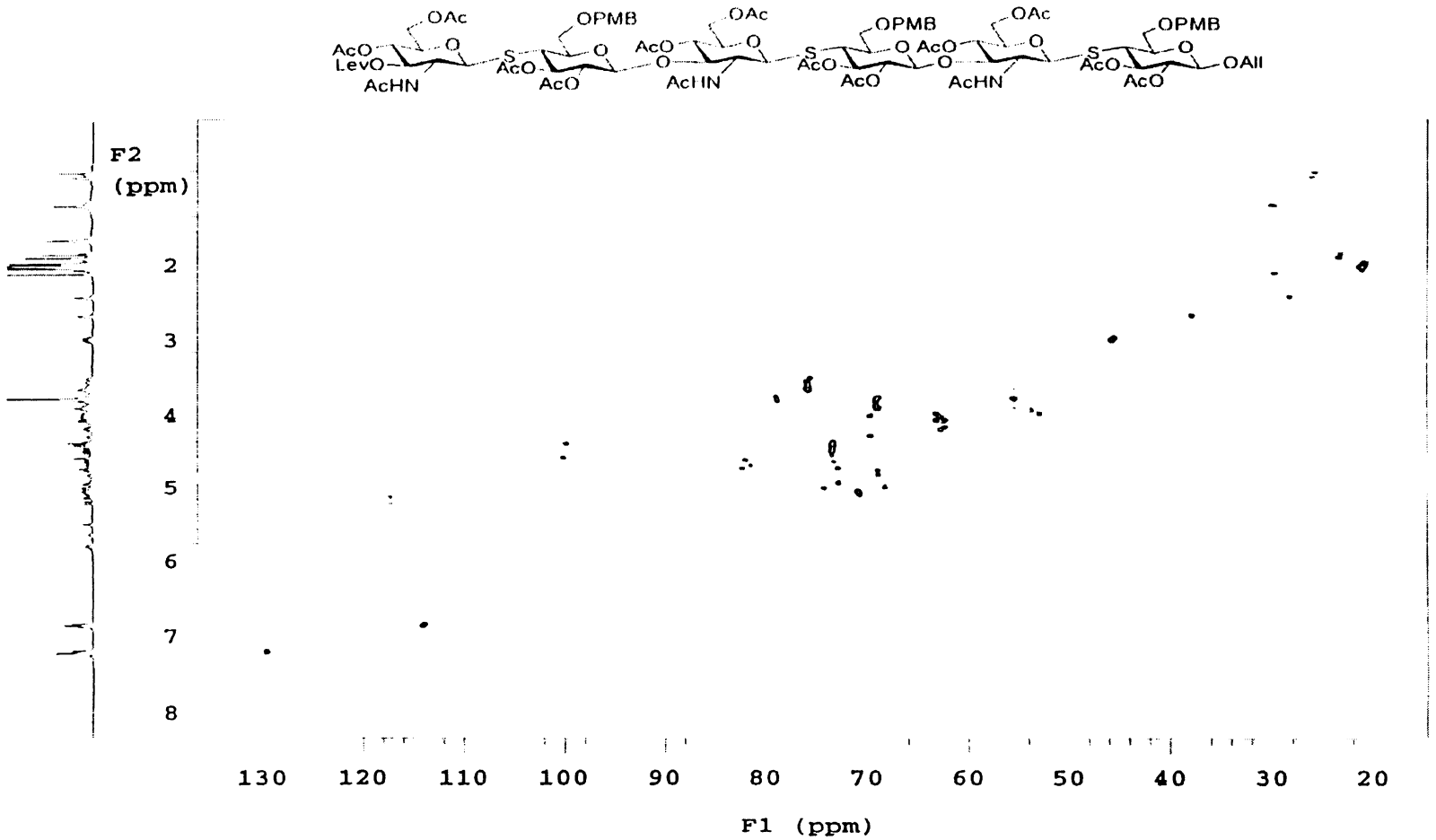
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**130**).



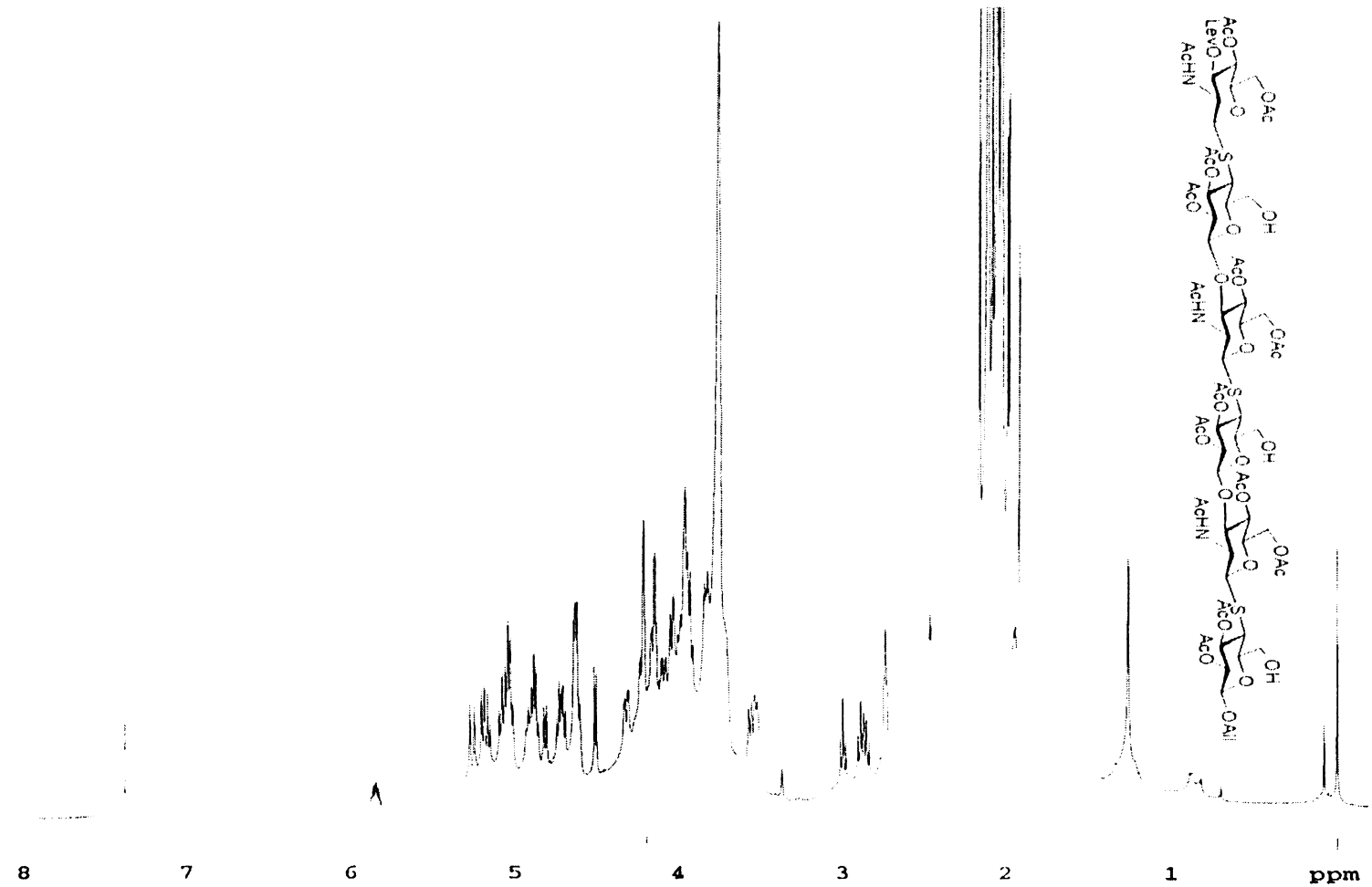
gCOSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**130**).



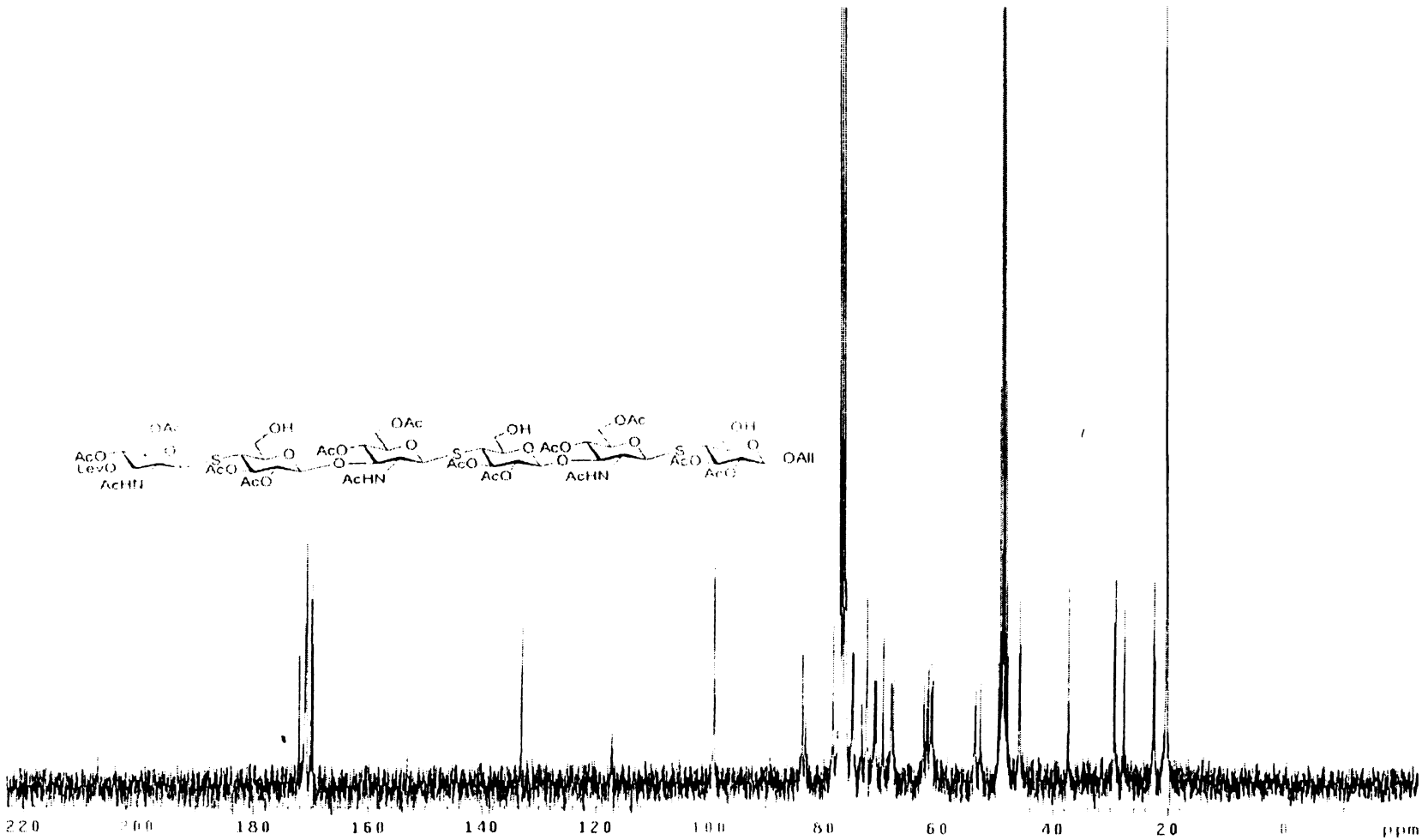
TOCSY spectrum (600 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**130**).



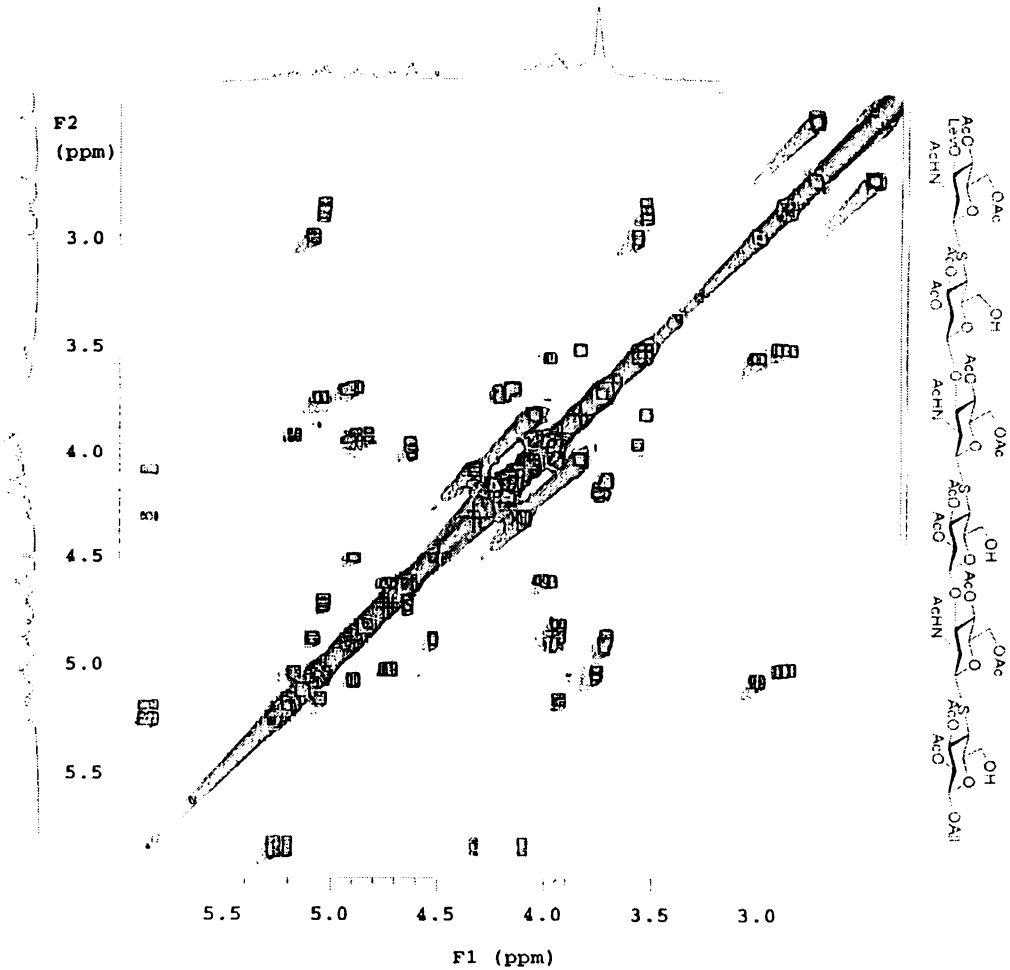
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3$) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-6-*O*-*p*-methoxybenzyl-4-thio-*β*-D-glucopyranoside (**130**).



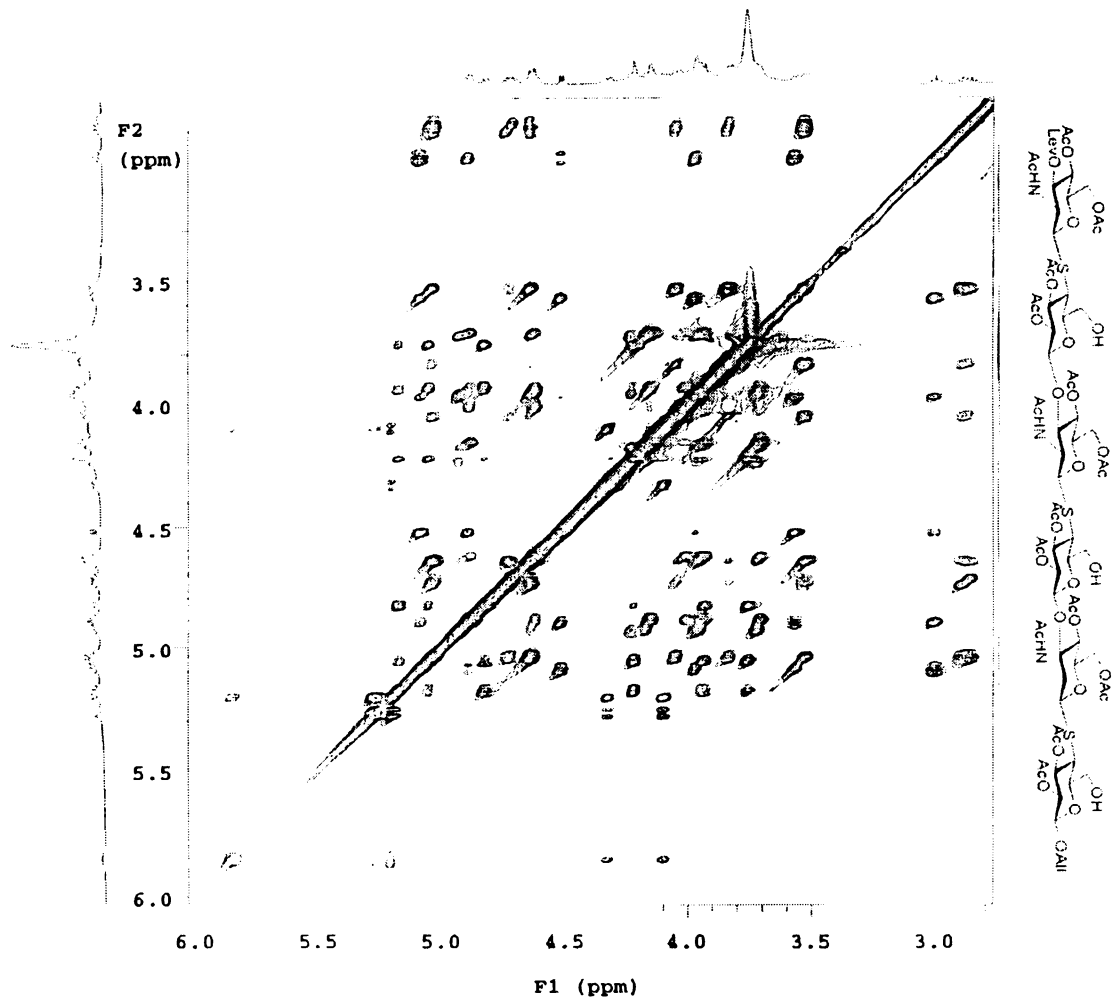
^{1}H NMR spectrum (600 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranoside (**131**).



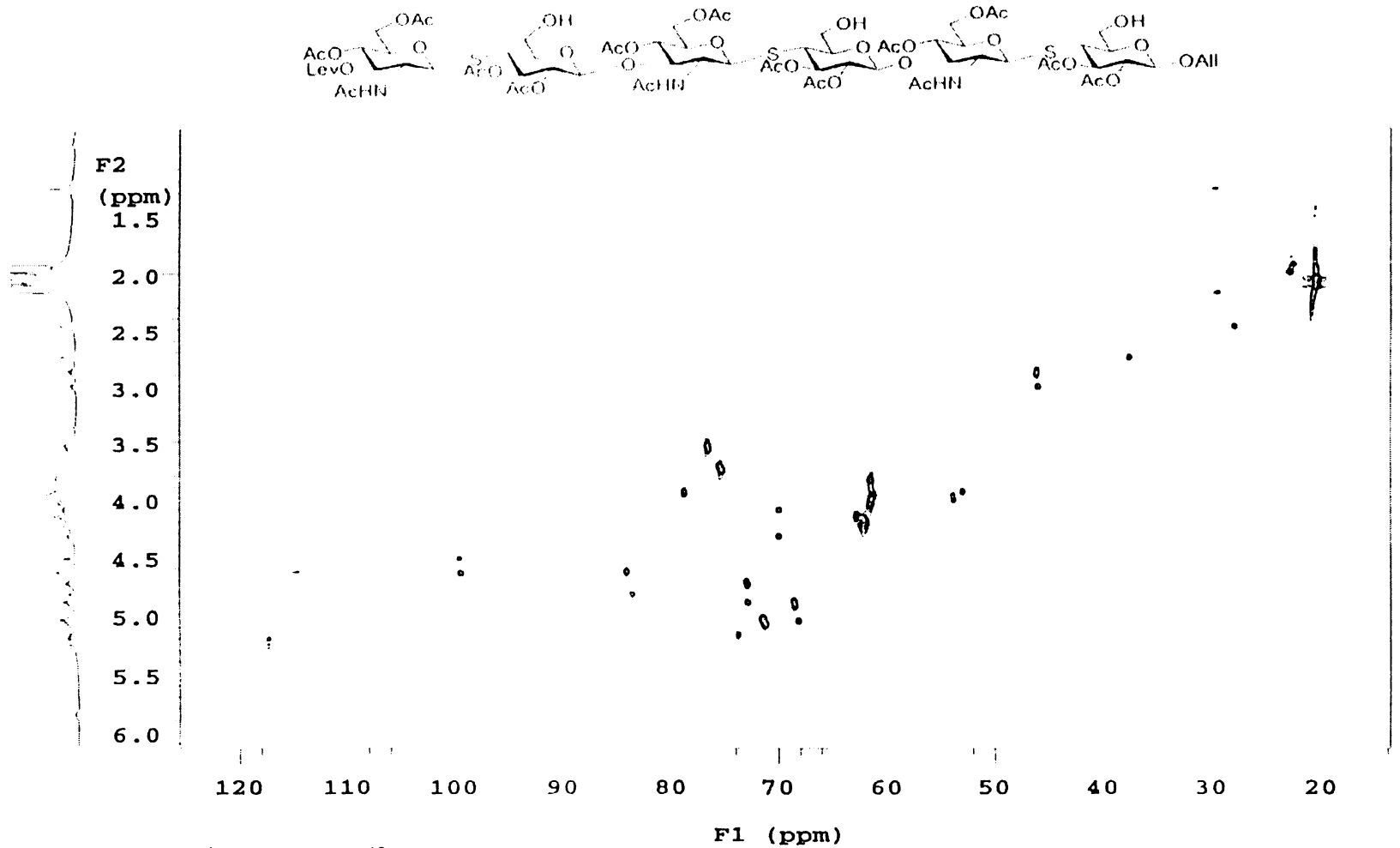
^{13}C NMR spectrum (75 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranoside (**131**).



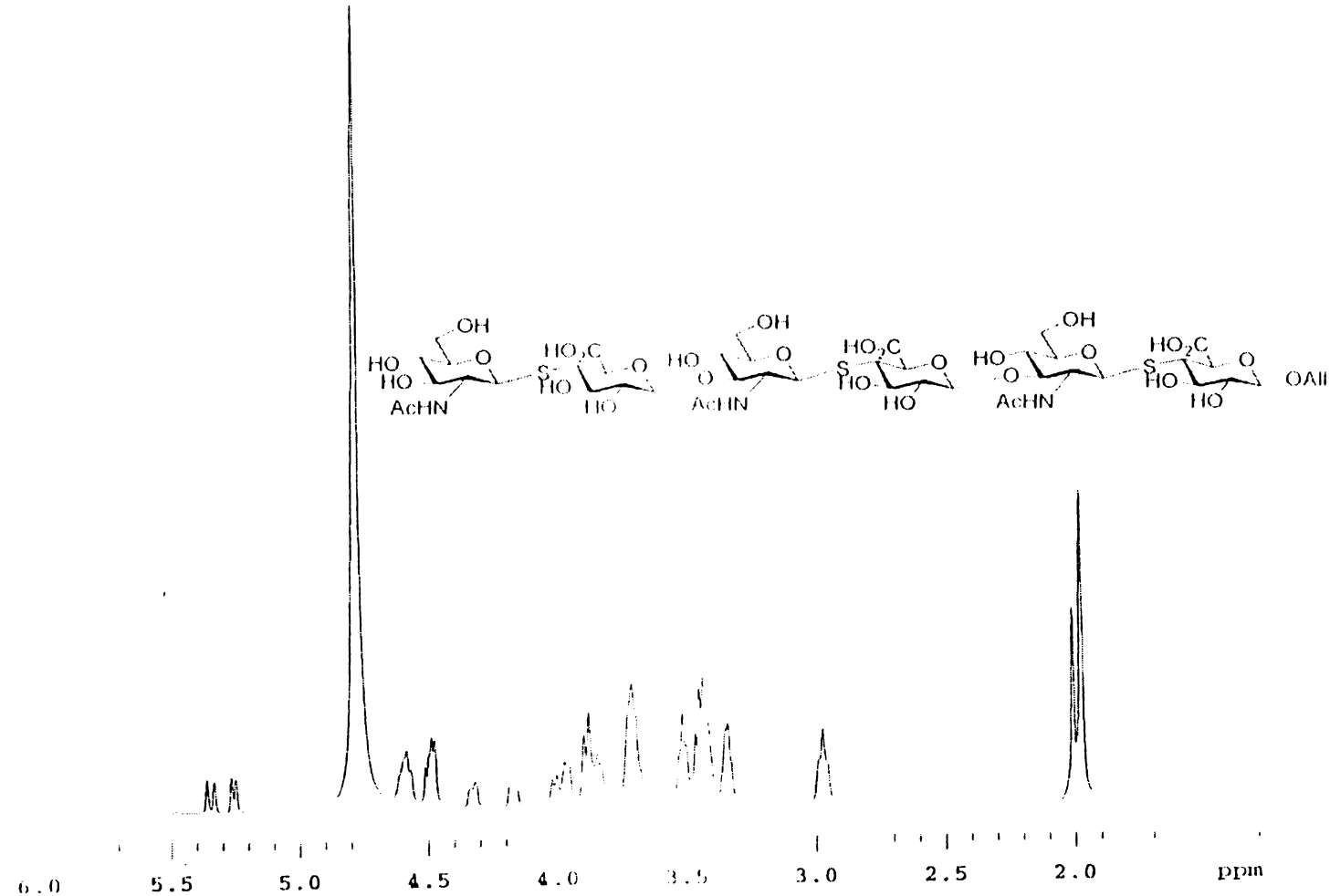
gCOSY spectrum (600 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranoside (**131**).



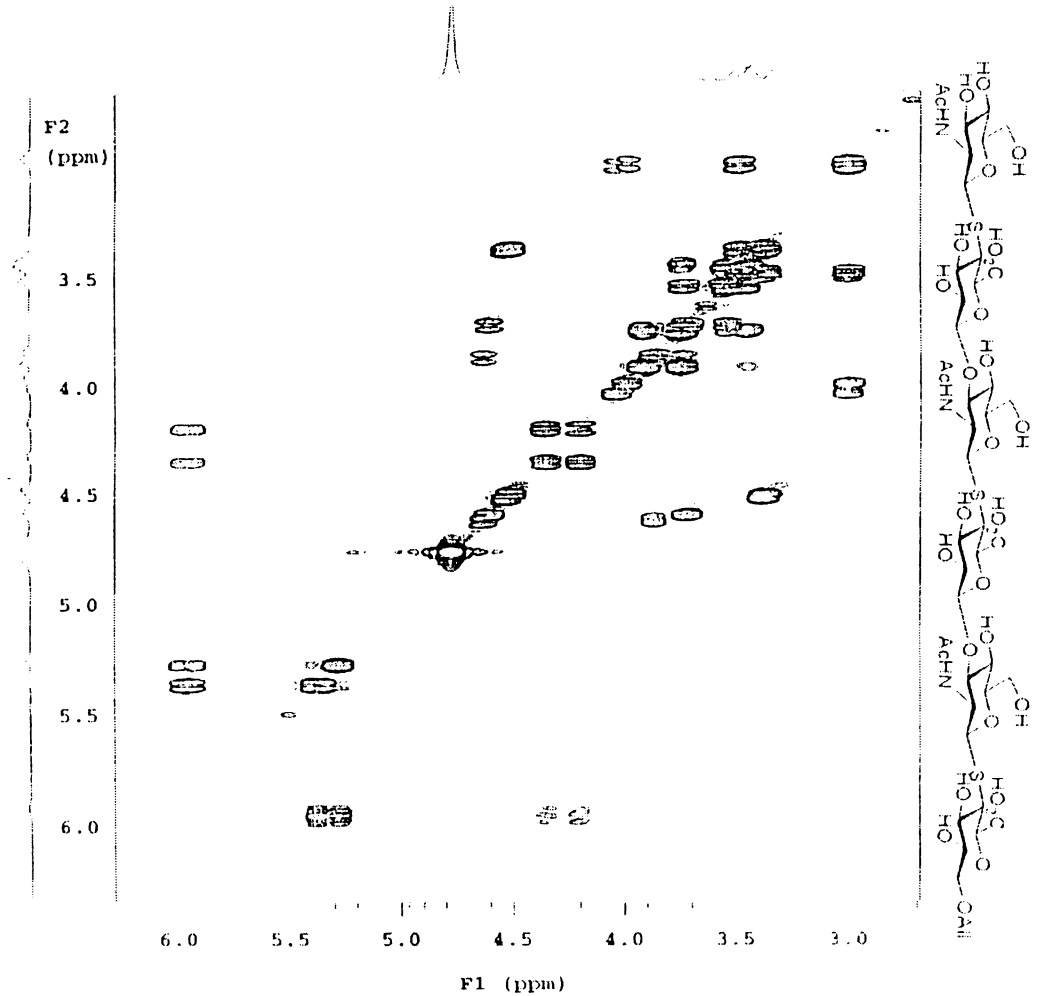
TOCSY spectrum (600 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranoside (**131**).



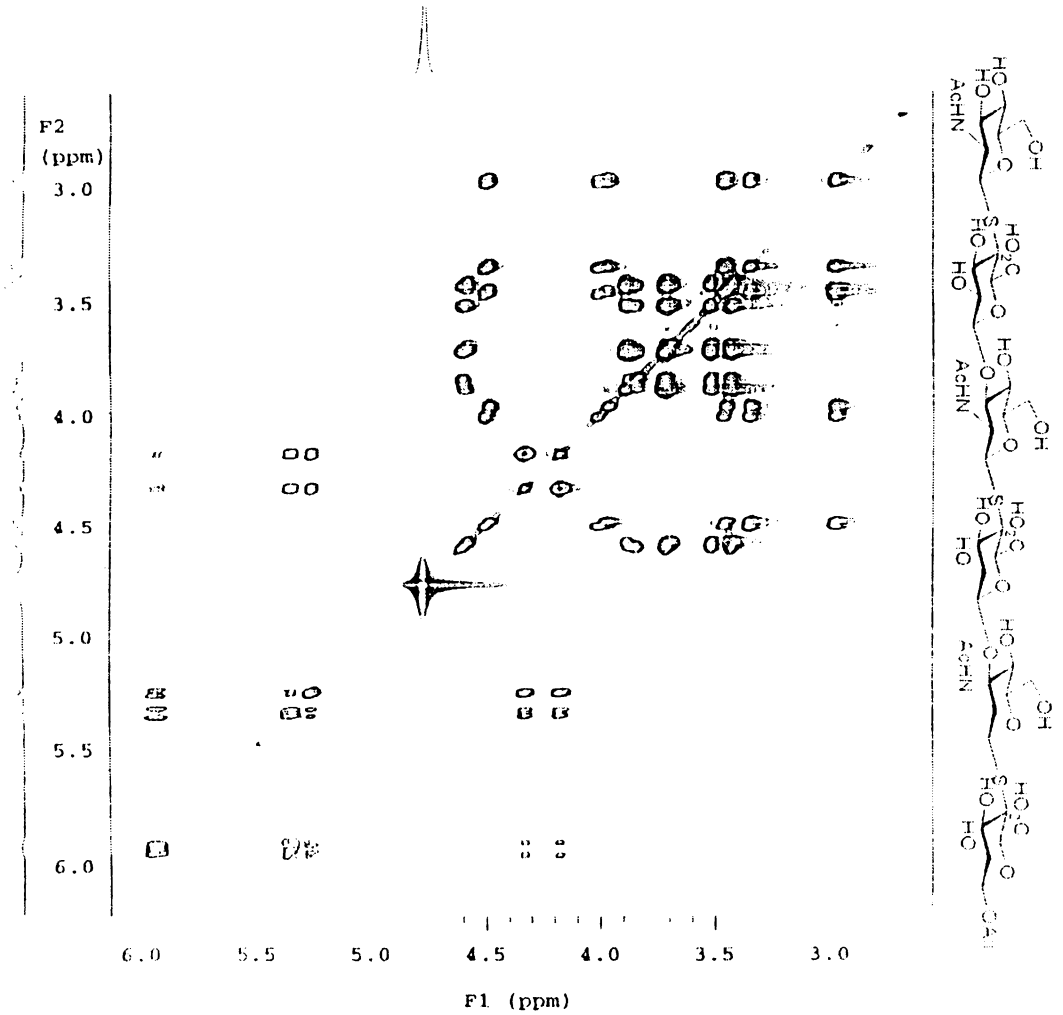
HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, $CDCl_3/CD_3OD$ = 5:1) of allyl *S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-levulinoyl-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranosyl)-(1→3)-*S*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-4-thio-*β*-D-glucopyranoside (**131**).



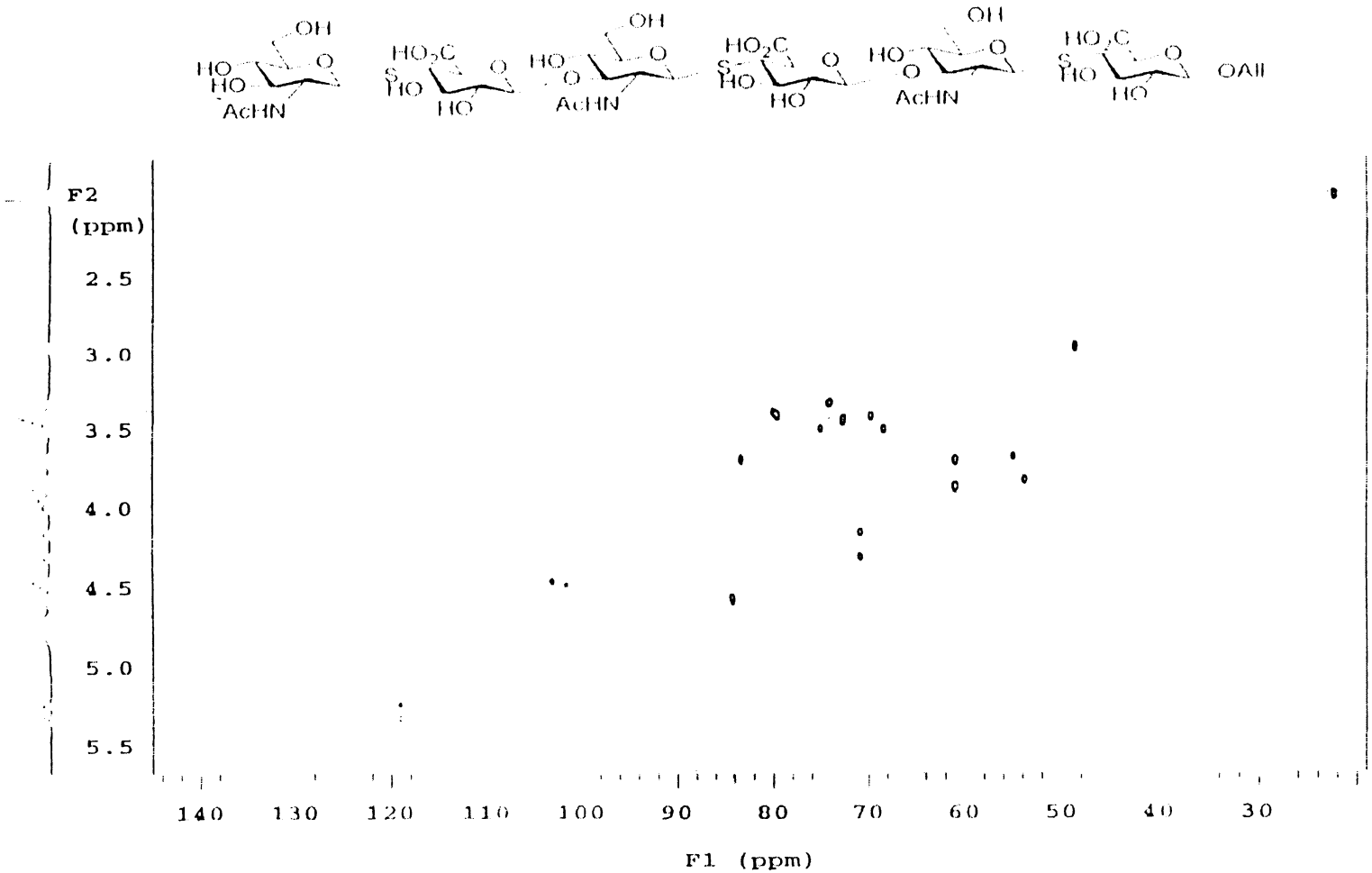
^{1}H NMR spectrum (600 MHz, D_2O) of allyl *S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-4-thio-*β*-D-glucopyranosiduronic acid (**133**).



gCOSY spectrum (600 MHz, D_2O) of allyl *S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-4-thio-*β*-D-glucopyranosiduronic acid (**133**).



TOCSY spectrum (600 MHz, D_2O) of allyl *S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-(4-thio-β-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-(4-thio-β-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-4-thio-β-D-glucopyranosiduronic acid (**133**).



HSQC spectrum (^{1}H: 600 MHz, ^{13}C: 150 MHz, D_2O) of allyl *S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-(4-thio-*β*-D-glucopyranosyluronic acid)-(1→3)-*S*-(2-acetamido-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-4-thio-*β*-D-glucopyranosiduronic acid (**133**).

VITA

Qiang Yang was born in AnHui, China in 1974. After graduating from Xiao Cheng No. 1 High School in AnHui in 1992, he attended Beijing Normal University, where he graduated with a Bachelor's degree in Chemistry. From 1996 to 1999 he studied at the Institute of Chemistry, Chinese Academy of Sciences, and conducted research in the synthesis of heterocyclic compounds and carbohydrates with Professor ZhanJiang Li, earning the Master's degree in Organic Chemistry. In 1999, he began graduate studies at the University of Tennessee, Knoxville, and joined the research group of Professor David C. Baker, where he conducted research in the synthesis of complex carbohydrates. After completing his PhD at UTK in 2002, he accepted a position in the Chemical Development Department at Albany Molecular Research, Inc. in Albany, New York.